



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : C12Q 1/68	A2	(11) International Publication Number: WO 00/50639 (43) International Publication Date: 31 August 2000 (31.08.00)
(21) International Application Number: PCT/US00/01392 (22) International Filing Date: 20 January 2000 (20.01.00) (30) Priority Data: 60/121,047 22 February 1999 (22.02.99) US 60/139,440 15 June 1999 (15.06.99) US 09/357,743 20 July 1999 (20.07.99) US (71) Applicant (for all designated States except US): VARIAGEN-ICS, INC. [US/US]; 60 Hampshire Street, Cambridge, MA 02139-1562 (US). (72) Inventor; and (75) Inventor/Applicant (for US only): STANTON, Vincent, Jr. [US/US]; 32 Royal Road, Belmont, MA 02173 (US). (74) Agents: WARBURG, Richard, J. et al.; Lyon & Lyon LLP, 633 West Fifth Street, Suite 4700, Los Angeles, CA 90071-2066 (US).		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>Without international search report and to be republished upon receipt of that report.</i>
(54) Title: GENE SEQUENCE VARIATIONS WITH UTILITY IN DETERMINING THE TREATMENT OF DISEASE (57) Abstract <p>The present disclosure describes the use of genetic variance information for genes involved in gene pathways in the selection of effective methods of treatment of a disease or condition. The variance information is indicative of the expected response of a patient to a method of treatment. Methods of determining relevant variance information and additional methods of using such variance information are also described.</p>		

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

DESCRIPTION

GENE SEQUENCE VARIATIONS WITH UTILITY IN DETERMINING THE TREATMENT OF DISEASE

BACKGROUND OF THE INVENTION

This application concerns the field of mammalian therapeutics and the selection of therapeutic regimens utilizing host genetic information, including gene sequence variances within the human genome in human populations.

The information provided below is not admitted to be prior art to the present invention, but is provided solely to assist the understanding of the reader.

Many drugs or other treatments are known to have highly variable safety and efficacy in different individuals. A consequence of such variability is that a given drug or other treatment may be effective in one individual, and ineffective or not well-tolerated in another individual. Thus, administration of such a drug to an individual in whom the drug would be ineffective would result in wasted cost and time during which the patient's condition may significantly worsen. Also, administration of a drug to an individual in whom the drug would not be tolerated could result in a direct worsening of the patient's condition and could even result in the patient's death.

For some drugs, over 90% of the measurable variation in selected pharmacokinetic parameters has been shown to be heritable. For a limited number of drugs, geneDNA sequence variances have been identified in specific genes that are involved in drug action or metabolism, and these variances have been shown to account for the variable efficacy or safety of the drugs in different individuals. As the sequence of the human genome is completed, and as additional human gene sequence variances are identified, the power of genetic methods for predicting drug response will further increase.

In this invention, we address the difficulties that arise in treating the following disease categories: 1) neurological and psychiatric disease; 2) pharmacokinetic and dynamic indices including efficacy, absorption, distribution, metabolism, and excretion, as well as safety and toxicity parameters; 3) inflammation and immune disease; 4) endocrine and metabolic disease; 5) cardiovascular and renal disease; and 6) cancer.

Neurological and Psychiatric Disease

Diseases of the central nervous system (CNS) present unique medical challenges to clinicians, patients, and caregivers. These diseases often progress to severely debilitating conditions. Further, the efficacy of available treatments is limited and there are serious, mostly unpredictable, side effects associated with some drugs. The progressive nature of neurological and psychiatric disease makes the passage of time a crucial issue in the treatment process. Specifically, selection of optimal treatment for neurological and psychiatric diseases is complicated by the fact that it often takes weeks or months to determine if a given therapy is symptomologyproducing a measurable benefit. Thus the current empirical approach to prescribing pharmacotherapy, in which each course of treatment for a given patient is a small experiment, is unsatisfactory from both a medical and economic perspective. Even when an effective treatment is ultimately identified, it often follows a period of ineffective or suboptimal treatment.

Pharmacokinetic and Pharmacodynamic Effects

The efficacy of a drug is a function of both pharmacodynamic effects and pharmacokinetic effects, or bioavailability. In the present invention, interpatient variability in drug safety, tolerability and efficacy are discussed in terms of the genetic determinants of interpatient variation in absorption, distribution, metabolism, and excretion, i.e. pharmacokinetic parameters.

Adverse drug reactions are a principal cause of the low success rate of drug development programs (less than one in four compounds that enters human clinical testing is ultimately approved for use by the US Food and Drug Administration (FDA)). Adverse drug reactions can be categorized as 1) mechanism based reactions and 2) idiosyncratic, "unpredictable" effects apparently unrelated to the primary pharmacologic action of the compound. Although some side effects appear shortly after administration, in some instances side effects appear only after a latent period. Adverse drug reactions can also be categorized into reversible and irreversible effects. The methods of this invention are useful for identifying the genetic basis of both mechanism based and 'idiosyncratic' toxic effects, whether reversible or not. Methods for identifying the genetic sources of interpatient variation in efficacy and mechanism based toxicity may be initially directed to analysis of genes affecting pharmacokinetic parameters, while the genetic causes of idiosyncratic adverse drug reactions are more likely to be attributable to genes affecting variation in pharmacodynamic responses or immunological responsiveness.

Absorption is the first pharmacokinetic parameter to consider when determining the causes of intersubject variation in drug response. The relevant genes depend on the route of administration of the compound being evaluated. For

orally administered drugs the major steps in absorption may occur during exposure to salivary enzymes in the mouth, exposure to the acidic environment of the stomach, exposure to pancreatic digestive enzymes and bile in the small intestine, exposure to enteric bacteria and exposure to cell surface proteins throughout the gastrointestinal tract. For example, uptake of a drug that is absorbed across the gastrointestinal tract by facilitated transport may vary on account of allelic variation in the gene encoding the transporter protein. Many drugs are lipophilic (a property which promotes passive movement across biological membranes). Variation in levels of such drugs may depend, for example, on the enterohepatic circulation of the drug, which may be affected by genetic variation in liver canalicular transporters, or intestinal transporters; alternatively renal reabsorption mechanisms may vary among patients as a consequence of gene sequence variances. If a compound is delivered parenterally then absorption is not an issue, however transcutaneous administration of a compound may be subject to genetically determined variation in skin absorptive properties.

Once a drug or candidate therapeutic intervention is absorbed, injected or otherwise enters the bloodstream it is distributed to various biological compartments via the blood. The drug may exist free in the blood, or, more commonly, may be bound with varying degrees of affinity to plasma proteins. One classic source of interpatient variation in drug response is attributable to amino acid polymorphisms in serum albumin, which affect the binding affinity of drugs such as warfarin. Consequent interpatient variation in levels of free warfarin have a significant effect on the degree of anticoagulation. From the blood a compound diffuses into and is retained in interstitial and cellular fluids of different organs to different degrees. Interpatient variation in the levels of a drug in different anatomical compartments may be attributable to variation in the genetically encoded chemical environment of those tissues (cell surface proteins, matrix proteins, cytoplasmic proteins and other factors)

Once absorbed by the gastrointestinal tract, compounds encounter detoxifying and metabolizing enzymes in the tissues of the gastrointestinal system. Many of these enzymes are known to be polymorphic in man and account for well studied variation in pharmacokinetic parameters of many drugs. Subsequently compounds enter the hepatic portal circulation in a process commonly known as first pass. The compounds then encounter a vast array of xenobiotic detoxifying mechanisms in the liver, including enzymes which are expressed solely or at high levels only in liver. These enzymes include the cytochrome P450s, glucuronyltransferases, sulfotransferases, acetyltransferases, methyltransferases, the glutathione conjugating system, flavine monooxygenases, and other enzymes known

in the art. Polymorphisms have been detected in all of these metabolizing systems, however the genetic factors responsible for intersubject variation have only been partially identified, and in some cases not yet identified at all. Biotransformation reactions in the liver often have the effect of converting lipophilic compounds into hydrophilic molecules which are then more readily excreted. Variation in these conjugation reactions may affect half-life and other pharmacokinetic parameters. It is important to note that metabolic transformation of a compound not infrequently gives rise to a second or additional compounds that have biological activity greater than, less than, or different from that of the parent compound. Metabolic transformation may also be responsible for producing toxic metabolites.

Biotransformation reactions can be divided into two phases. Phase I are oxidation-reduction reactions and phase II are conjugation reactions. The enzymes involved in both of these phases are located predominantly in the liver, however biotransformation can also occur in the kidney, gastrointestinal tract, skin, lung and other organs. Phase I reactions occur predominantly in the endoplasmic reticulum, while phase II reactions occur predominantly in the cytosol. Both types of reactions can occur in the mitochondria, nuclear envelope, or plasma membrane. One skilled in the art can, for some compounds, make reasonable predictions concerning likely metabolic systems given the structure of the compound. Experimental means of assessing relevant biotransformation systems are also described.

Drug-Induced Disease, Disorders or Toxicities

Drug-induced disease or toxicity presents a unique series of challenges to drug developers, as these reactions are often not predictable from preclinical studies and may not be detected in early clinical trials involving small numbers of subjects. When such effects are detected in later stages of clinical development they often result in termination of a drug development program because, until now, there have been no effective tools to seek the determinants of such reactions. When a drug is approved despite some toxicity its clinical use is frequently severely constrained by the possible occurrence of adverse reactions in even a small group of patients. The likelihood of such a compound becoming first line therapy is small (unless there are no competing products). Thus clinical trials that lead to detection of genetic causes of adverse events and subsequently to the creation of genetic tests to identify and screen out patients susceptible to such events have the potential to (i) enable approval of compounds for genetically circumscribed populations or (ii) enable repositioning of approved compounds for broader clinical use.

Similarly, many compounds are not approved due to unimpressive efficacy. The identification of genetic determinants of pharmacokinetic variation may lead to identification of a genetically defined population in whom a significant response is

occurring. Approval of a compound for this population, defined by a genetic diagnostic test, may be the only means of getting regulatory approval for a drug. As healthcare becomes increasingly costly, the ability to allocate healthcare resources effectively becomes increasingly urgent. The use of genetic tests to develop and rationally administer medicines represents a powerful tool for accomplishing more cost effective medical care.

Inflammation and Immune Disease

In this application, we further address the difficulties that arise in treating inflammatory diseases and other diseases in which modulation of immunologic function provides the basis for therapeutic intervention, including, for example, diseases treated with antiinflammatory, analgesic or antipyretic drugs as well as autacoids, eicosanoids, interleukins, cytokines or their agonists or antagonists. Diseases or conditions involving the inflammatory response or immune system constitute a complex and heterogeneous group of diseases, involving all organ systems from the central nervous system and the circulatory system to the viscera and skin. The diseases may be acute or chronic, or may have an acute stage which later progresses to a chronic condition, or may exhibit a waxing and waning pattern of flare ups and remissions. Due to their wide anatomical distribution, this group of diseases can (collectively) lead to impairment of a wide range of essential physiological functions. The unifying theme in the treatment of these diseases is the modulation of inflammatory mediators or immune function.. The evaluation of long term response to therapy is, for many of these diseases, the most important index of treatment efficacy, due to the progressive nature of inflammatory or immunological diseases. Since it is often difficult to assess the long term effects of treatment over a short observation period (particularly for diseases with a waxing and waning pattern) there is considerable utility in a genetic test that can predict long term outcomes. Many treatments for diseases with significant inflammatory or immunological components are quite costly.

Endocrine and Metabolic Disease

The endocrine system encompasses a number of organs that collectively regulate a wide array of physiologic, metabolic and developmental processes including metabolism, growth, reproduction, development, senescence, behavior, including adaptation to stress, the composition of intracellular and extracellular fluids (e.g. salt and water balance), digestion and wound healing, among other processes. The endocrine organs include the hypothalamus, pituitary gland, thyroid, parathyroid, endocrine pancreas, adrenal gland, gonads, and cells of the gastrointestinal tract, liver, kidneys, heart, pineal gland, and placenta.

Endocrine signals can be classified as autocrine, paracrine, or endocrine depending on the distance over which a signal must be transmitted. Endocrine signals are transmitted by hormones including peptides, proteins, steroids and small molecule neurotransmitters. The hormones carry biological signals to target cells. Receptors located on the cell surface (membrane bound) activate intracellular second messenger systems to ultimately alter intracellular metabolism, physiology and cell function. Second messengers systems include adenylate cyclase, guanylate cyclase, phospholipases, and kinases. Some membrane receptors interact with GTP-binding proteins; others produce intracellular signals themselves (for example receptors with tyrosine kinase domains). Other receptors are located intracellularly (for example steroid hormone receptors) and the hormone-receptor complex acts to stimulate intracellular processes such as gene transcription.

Regulation in the endocrine system occurs via a complex system of signals transmitted by hormones, neurotransmitters and other small molecules. These signals participate in feedback loops, recruitment of coordinate responses, and cycles or rhythms. The feedback loops function to coordinately stimulate or terminate hormone signals. In this way, communication occurs between cells or tissues that are physically separated. For example, a peripheral endocrine gland may release hormones in response to centrally produced stimulatory hormones, with the peripherally produced substances feeding back on the central nervous system to decrease production of the stimulatory signal. In other systems the action of multiple hormones must be coordinated. For example, female reproductive system requires hypothalamic, pituitary and ovarian signals and also includes effector targets in the breasts, uterus, and vagina. Endocrine signalling systems that are regulated in a coordinated fashion include, for example, the hypothalamic-pituitary-gonadal axis, the hypothalamic-pituitary-adrenal corticotroph axis and the hypothalamic-pituitary-thyroid axis. Within the endocrine system there is integration of endocrine responses that are grouped as.

Many hormones are extensively processed prior to secretion. For example in the posterior pituitary gland, a hormone gene encodes a preprohormone that contains several proteins or peptides in contiguous alignment that requires modification prior to becoming an active signaling hormone. The preprohormone after nascent ribosome synthesis then is cut by specific or nonspecific processing proteins to a smaller prohormone within the Golgi apparatus, that then is glycosylated and placed into a secretory granule. Within the secretory granule, the prohormone is then further processed into the active hormone. The active hormone is secreted as a response to physiologic signals and renders the specific biologic function at the target organ or tissue. In this complex protein processing mechanism, there is the

possibility of secreting more than one hormones or signaling peptides in the same secretory granule, and as described above, can lead to the delivery of multiple signals to one or more target tissues.

Assessment of endocrine function can be conducted by quantitation of circulating hormones and metabolic products, stimulation and suppression tests, and anatomic assessment. Aberrations of endocrine disease, disorder, or dysfunction manifests clinically as either a deficiency or a excess of 1) endocrine function or 2) hormone production, or may be the result of loss of 1) feedback loops, 2) recruitment of hormone signals, or 3) cycles or pulsatile hormone secretion. Lastly, there may be genetic determinants of endocrine disease, for example mutations or polymorphisms in biosynthetic enzymes, hormone receptors, peptide hormone or small molecules, immune surveillance, tumor suppressor genes, and others such that these changes or differences from normally occurring proteins or molecules alters their functional pattern and the clinical manifestation is then characteristic of endocrine disease.

Endocrine or metabolic disease provide a unique series of complications for clinicians, patients, and care givers; the diseases often progress rapidly and disrupts a vast number of major life functions. The progressive nature of these disease syndromes makes the passage of time a crucial issue in the treatment process.

Treatment choices for endocrine or metabolic disorders and their associated pathologies, particularly those affecting major organs, e.g. coronary, hepatic, renal systems, are often complicated by the fact that it often takes a significant period of treatment to determine if a given therapy is effective. Accordingly, treatment with the most effective drug or drugs is often delayed while the disease continues to progress. A method that would allow one to predict which patients will respond to a specific therapy would provide physical and psychological benefits. As healthcare becomes increasingly inaccessible, the ability to allocate healthcare resources effectively also becomes more important.

Cardiovascular and Renal Disease

In this application, we address the difficulties that arise in treating cardiovascular and renal diseases, describe methods to enable more effective use of available therapeutics, and methods for developing new therapies. Diseases of the cardiovascular and renal systems often progress, over periods of years to decades, to severely debilitating and life threatening conditions. The efficacy of available treatments is limited and there are side effects associated with many of the drugs used to treat these diseases. Due to the progressive nature of many cardiovascular and renal diseases it is of great importance to select an effective therapeutic regimen at the time of diagnosis. The effectiveness of therapy is often

assessed by short-term measurements of surrogate markers (e.g. blood pressure, blood lipid levels or blood clotting parameters), however the important endpoints (e.g. myocardial infarction, thromboembolism, renal failure) occur (or are prevented) over the long term. Thus, the tools for selecting optimal therapy for individual patients are currently limited, and as a result some patients receive treatment from which they do not benefit, while other patients may not receive treatment that would produce significant benefit. The current empirical approach to prescribing pharmacotherapy, in which each course of treatment for a given patient is a small experiment (e.g. the selection of effective therapy for blood pressure control), is unsatisfactory from both a medical and economic perspective. Even when an effective treatment is ultimately identified, it often follows a period of ineffective or suboptimal treatment. Methods that would help caregivers predict which patients will exhibit beneficial therapeutic responses to which medications would provide both medical and economic benefits. As healthcare becomes increasingly costly, the ability to rationally allocate healthcare expenditures, and in particular pharmacy resources, becomes increasingly important. The methods of this invention provide a basis for selecting more efficacious pharmacotherapy of cardiovascular and renal diseases.

Neoplastic Disorders

In this application, we also address the difficulties that arise in treating neoplastic disease. Due to the often rapid progression and life-threatening nature of neoplastic diseases, both early detection and effective treatment are essential. Clearly, there would be great benefit to patients if therapies that will ultimately prove to be ineffective in curbing the progression of disease could be avoided initially, given the cost and often noxious side effects associated with such therapies. Many current therapies for neoplastic disease are targeted against processes such as cell growth and division that occur in both normal and cancerous tissues (albeit at different rates), resulting in pronounced toxicity to normal tissues. Toxic reactions are the most severe in tissues which proliferate rapidly, such as gastrointestinal epithelium and hematopoietic tissues, however serious adverse reactions also occur in other organs occasionally, including heart, kidney, liver, lung and brain. As a consequence of the narrow therapeutic index associated with most antineoplastic treatments, skillful choice of treatments (including the agents used and the dose, if the treatment involves drugs) must be made by the attending physician based not only upon the type of cancer and stage of dissemination, but on a number of additional factors including status of the patient's hematopoietic and myelogenic tissues, hepatic and renal function and age. Knowledge of genetic factors which would impact the choice of treatment based either on optimizing efficacy or

minimizing toxicity would greatly benefit cancer patients, because the efficacy of available treatments is limited and there are serious, mostly unpredictable, side effects associated with some drugs. Thus a method that would allow one to predict which patients will exhibit beneficial therapeutic response to a specific medication with minimal adverse effects (often less than half of treated patients, and not infrequently one quarter or less) would provide physical, psychological, and societal benefits. Using such a method, those patients not likely to benefit from aggressive treatment could be offered palliative care. Tumor growth exhibits gompertzian kinetics—growth rate declines with increasing tumor burden. Since chemotherapies are frequently most effective against rapidly growing tumors (low tumor burden), it is imperative that treatment begin immediately after disease detection and that the tumor responds to first-line therapy. Further, selection of optimal treatment for a neoplastic disease is complicated by the fact that it often takes weeks or months to determine if a given therapy is producing a measurable benefit. Thus the current empirical approach to prescribing pharmacotherapy, in which each course of treatment for a given patient is a small experiment, is unsatisfactory from both a medical and economic perspective. Even when an effective treatment is ultimately identified, it often follows a period of ineffective or suboptimal treatment.

Neoplastic diseases are related by the fact that they result from the unchecked growth of a previously normal cell, generally thought to be precipitated by one or more mutations in its genetic material. Cancerous cells can undergo gene loss and duplication to become aneuploid or partially polyploid, but usually retain some of the characteristics of their source tissue. Neoplastic cells differ in their ability to form solid tumors, to disseminate from the original site of tumor formation and form metastases, and in their requirements for growth factors, which can include steroid hormones in the case of carcinomas of the prostate or breast. Tumor cells, while having sustained alterations to their genetic material that lead either to a loss of growth inhibition or to a gain of growth function, still produce all the enzymes and other macromolecules required for cell viability. In this regard, they are extremely similar to non-cancerous tissue, and selective poisoning of tumor tissue over normal tissue has for the most part proven elusive. Current chemotherapies mainly target normal cell functions including DNA replication, cell division, RNA transcription, and nucleotide metabolism and are often associated with nausea and vomiting, diarrhea, hair loss, anemia, immune suppression (and consequent increased risk of infection), as well as a host of less common side effects including pulmonary fibrosis, and cardiac, hepatic and renal toxicity. Radiation therapy, often used in the treatment of inoperable tumors such as various brain and laryngeal tumors (but also widely used to treat breast cancer in patients who have had

lumpectomies), has the advantage that it can be restricted to a small area, especially when used in conjunction with tissue selective radiosensitizers or radioprotectants. Radiation therapy also targets rapidly proliferating tissues and shares many of the side effects of cytotoxic agents. Minimization of severe toxic reactions to cancer therapy through knowledge of genetic variances in normal tissue that could impact either drug metabolism or cellular repair processes would be an invaluable addition to cancer therapy.

Accordingly, a method that would help caregivers predict which patients will exhibit beneficial therapeutic responses to a specific which medication or medications would provide both medical and economic benefits. As healthcare becomes increasingly costly, the ability to rationally allocate healthcare expenditures, and in particular pharmacy resources, also becomes increasingly important.

SUMMARY OF THE INVENTION

The present invention is concerned generally with the field of identifying an appropriate treatment regimen for a neurological or psychiatric disease, drug-induced disease or disorders, endocrine or metabolic disease, inflammatory disease (or a disease in which modulation of the inflammatory response or the immune system is being tested for therapeutic effect), and cardiovascular and renal diseases, based upon genotype in mammals, particularly in humans. The present invention is additionally concerned generally with the field of pharmacology, specifically pharmacokinetics and toxicology, and more specifically with identifying and predicting inter-patient differences in response to drugs in order to achieve superior efficacy and safety in selected patient populations.

It is further concerned with the genetic basis of inter-patient variation in response to therapy, including drug therapy, and with methods for determining and exploiting such differences to improve medical outcomes. Specifically, this invention describes the identification of genes and gene sequence variances useful in the field of therapeutics for optimizing efficacy and safety of drug therapy by allowing prediction of pharmacokinetic and/or toxicologic behavior of specific drugs in specific patients. Relevant pharmacokinetic processes include absorption, distribution, metabolism and excretion. Relevant toxicological processes include both dose related and idiosyncratic adverse reactions to drugs, including, for example, hepatotoxicity, blood dyscrasias and immunological reactions.

It is further concerned with the genetic basis of inter-patient variation in response to therapy, including drug therapy. Specifically, this invention describes the identification of gene sequence variances useful in the field of therapeutics for optimizing efficacy and safety of drug therapy. These variances may be useful
5 either during the drug development process or in guiding the optimal use of already approved compounds. DNA sequence variances in candidate genes (i.e. genes that may plausibly affect the action of a drug) are tested in clinical trials, leading to the establishment of diagnostic tests useful for improving the development of new pharmaceutical products and/or the more effective use of existing pharmaceutical
10 products. Methods for identifying genetic variances and determining their utility in the selection of optimal therapy for specific patients are also described. In general, the invention relates to methods for identifying patient population subsets that respond to drug therapy with either therapeutic benefit or side effects (i.e. symptomatology prompting concern about safety or other unwanted signs or
15 symptoms).

This broad range of pharmacological interactions with receptors, transporters, enzymes and other proteins which are differentially expressed in different populations of cells, e.g., in the CNS, has implications for the design of experiments to identify genetic determinants of drug response. In particular, because
20 of the broad pharmacological interactions of compounds being developed as CNS drugs it may be necessary to study the effect of DNA sequence variances in a number of different sets of genes (belonging to different biochemical pathways) in order to identify a sequence variance or set of variances responsible for interpatient variation in drug response. Methods are described herein for identifying relevant
25 DNA sequence variances and associating them with drug response phenotypes.

While the complexity of CNS physiology creates challenges for pharmacogenetic studies, it is also the case that the pharmacological treatment of CNS diseases provides broad scope for the methods of this invention, because (i) the hereditary component of many CNS diseases is well established, indicating a major
30 role of genetic (as opposed to environmental) factors in disease etiology, (ii) the molecular pharmacology of CNS drugs is generally well understood, providing a rational basis for selecting genes for pharmacogenetic investigation (iii) the heterogeneous responses of patients to CNS drugs suggests that the factors governing response extend beyond presently understood mechanisms; genetic
35 variation can affect virtually all aspects of pharmacology, and is, for the reasons cited above, likely to account for much of the heterogeneity in drug response. In this application we describe methods for improving the treatment of neurological and psychiatric diseases, movement disorders, neurodegenerative diseases, disorders of

sensation, and cerebrovascular diseases. Specifically, we address the treatment of migraine, pain, epilepsy, schizophrenia, stroke, depression, anxiety, spasticity, Parkinson's disease, dementia, demyelinating disease, amyotrophic lateral sclerosis, and Huntington's disease.

5 Specifically, this invention describes the identification of genes and gene sequence variances useful in the field of therapeutics for optimizing efficacy and safety of drug therapy by allowing prediction of pharmacokinetic and/or toxicologic behavior of specific drugs in specific patients. Relevant pharmacokinetic processes include absorption, distribution, metabolism and excretion. Relevant toxicological
10 processes include both dose related and idiosyncratic adverse reactions to drugs, including, for example, hepatotoxicity, blood dyscrasias and immunological reactions.

The invention also describes methods for establishing diagnostic tests useful in (i) the development of, (ii) obtaining regulatory approval for and (iii) safe and
15 efficacious clinical use of pharmaceutical products. These variances may be useful either during the drug development process or in guiding the optimal use of already approved compounds. DNA sequence variances in candidate genes (i.e. genes that may plausibly affect the action of a drug) are tested in clinical trials, leading to the establishment of diagnostic tests useful for improving the development of new
20 pharmaceutical products and/or the more effective use of existing pharmaceutical products. Methods for identifying genetic variances and determining their utility in the selection of optimal therapy for specific patients are also described. In general, the invention relates to methods for identifying and dealing effectively with the genetic sources of interpatient variation in drug response, including both variable
25 efficacy as determined by pharmacokinetic variability and variable toxicity as determined by pharmacokinetic factors or by other genetic factors (e.g. factors responsible for idiosyncratic drug response).

This application is directed also to diseases in which abnormal function of the immune system or the inflammatory response is part of the disease process, or in
30 which modulation of immune or inflammatory function is being tested as a therapeutic intervention. Specifically we address the treatment of arthritis, chronic obstructive pulmonary disease, autoimmune disease, transplantation, pain associated with inflammation, psoriasis, atherosclerosis, asthma, inflammatory bowel disease, and hepatitis.

35 In this application we further describe methods for improving the treatment of endocrine and metabolic diseases. Specifically, we address the treatment of diabetes mellitus and the related metabolic syndrome X, diabetes insipidus, obesity, contraception and infertility, osteoporosis, acne, and alopecia. The methods of this

invention are also relevant to devising effective genetic approaches to drug development for endocrine diseases of pituitary, thyroid, parathyroid, adrenal, gonads and secondary sex tissues.

While the complexity of cardiovascular and renal physiology creates
5 challenges for pharmacogenetic studies (e.g. selecting the right genes to study, selecting the relevant DNA sequence variances within those genes, constructing sound genetic statistical tests, etc.), it is also the case that the pharmacological treatment of cardiovascular and renal diseases provides broad scope for the methods of this invention, because (i) the hereditary component of many cardiovascular and
10 renal diseases is well established, indicating a major role of genetic (as opposed to environmental) factors in disease etiology, (ii) the molecular pharmacology of cardiovascular and renal drugs is generally well understood, providing a rational basis for selecting genes for pharmacogenetic investigation (iii) the heterogeneous responses of patients to cardiovascular and renal drugs suggests that the factors
15 governing response extend beyond presently understood mechanisms; genetic variation can affect virtually all aspects of pharmacology, and are, for the reasons cited above, likely to account for much of the heterogeneity in drug response. In this application we describe methods for improving the treatment of cardiovascular and renal diseases. Specifically, we address the treatment of anemia, angina (including
20 coronary artery atherosclerosis), arrhythmias, hypertension, hypotension, myocardial ischemia, heart failure, thrombosis, renal diseases, restenosis, and peripheral vascular disease (including atherosclerosis). The methods of this invention are also relevant to devising effective genetic approaches to drug development for other cardiovascular and renal diseases.

25 Described in the Examples and Tables are pathways, genes and gene sequence variances useful in the genetic analysis of treatment response for each of these diseases, and exemplary compounds being developed to treat each of these diseases, the use of which may be improved by genetic analysis of the type described herein.

30 The inventors have determined that the identification of gene sequence variances in genes that may be involved in drug action are useful for determining whether genetic variances account for variable drug efficacy and safety and for determining whether a given drug or other therapy may be safe and effective in an individual patient. Provided in this invention are identifications of genes and
35 sequence variances which can be useful in connection with predicting differences in response to treatment and selection of appropriate treatment of a disease or condition. A target gene and variances are useful, for example, in pharmacogenetic association studies and diagnostic tests to improve the use of certain drugs or other

therapies including, but not limited to, the drug classes and specific drugs identified in the 1999 Physicians' Desk Reference (53rd edition), Medical Economics Data, 1998, the 1995 United States Pharmacopeia XXIII National Formulary XVIII, Interpharm Press, 1994, Tables 24-68 or other sources as described below.

5 The terms "disease" or "condition" are commonly recognized in the art and designate the presence of signs and/or symptoms in an individual or patient that are generally recognized as abnormal. Diseases or conditions may be diagnosed and categorized based on pathological changes. Signs may include any objective evidence of a disease such as changes that are evident by physical examination of a patient or the results of diagnostic tests which may include, among others, laboratory tests to determine the presence of DNA sequence variances or variant forms of certain genes in a patient. Symptoms are subjective evidence of disease or a patients condition, i.e. the patients perception of an abnormal condition that differs from normal function, sensation, or appearance, which may include, without limitations, physical disabilities, morbidity, pain, and other changes from the normal condition experienced by an individual. Various diseases or conditions include, but are not limited to; those categorized in standard textbooks of medicine including, without limitation, textbooks of nutrition, allopathic, homeopathic, and osteopathic medicine. In certain aspects of this invention, the disease or condition is selected from the group consisting of the types of diseases listed in standard texts such as Harrison's Principles of Internal Medicine (14th Ed) by Anthony S. Fauci, Eugene Braunwald, Kurt J. Isselbacher, et al. (Editors), McGraw Hill, 1997, or Robbins Pathologic Basis of Disease (6th edition) by Ramzi S. Cotran, Vinay Kumar, Tucker Collins & Stanley L. Robbins, W B Saunders Co., 1998, or the Diagnostic and Statistical Manual of Mental Disorders: DSM-IV (4th edition), American Psychiatric Press, 1994, or other texts described below. Examples for this invention include, neoplastic disorders such as cancer, amyotrophic lateral sclerosis, anxiety, dementia, depression, epilepsy, Huntington's disease, migraine, demyelinating disease, multiple sclerosis, pain, Parkinson's disease, schizophrenia, spasticity, psychoses, and stroke, drug-induced diseases, disorders, or toxicities consisting of blood dyscrasias, cutaneous toxicities, systemic toxicities, central nervous system toxicities, hepatic toxicities, cardiovascular toxicities, pulmonary toxicities, and renal toxicities, arthritis, chronic obstructive pulmonary disease, autoimmune disease, transplantation, pain associated with inflammation, psoriasis, atherosclerosis, asthma, inflammatory bowel disease, and hepatitis, diabetes mellitus, metabolic syndrome X, diabetes insipidus, obesity, contraception, infertility, hormonal insufficiency related to aging, osteoporosis, acne, alopecia, adrenal dysfunction, thyroid dysfunction, and parathyroid dysfunction, anemia,

angina, arrhythmia, hypertension, hypothermia, ischemia, heart failure, thrombosis, renal disease, restenosis, and peripheral vascular disease

In connection with the methods of this invention, unless otherwise indicated, the term "suffering from a disease or condition" means that a person is either
5 presently subject to the signs and symptoms, or is more likely to develop such signs and symptoms than a normal person in the population. Thus, for example, a person suffering from a condition can include a developing fetus, a person subject to a treatment or environmental condition which enhances the likelihood of developing the signs or symptoms of a condition, or a person who is being given or will be
10 given a treatment which increase the likelihood of the person developing a particular condition. For example, tardive dyskinesia is associated with long-term use of anti-psychotics; dyskinesias, paranoid ideation, psychotic episodes and depression have been associated with use of L-dopa in Parkinson's disease; (and dizziness, diplopia, ataxia, sedation, impaired mentation, weight gain, and other undesired effects have
15 been described for various anticonvulsant therapies. Thus, methods of the present invention which relate to treatments of patients (e.g., methods for selecting a treatment, selecting a patient for a treatment, and methods of treating a disease or condition in a patient) can include primary treatments directed to a presently active disease or condition, secondary treatments which are intended to cause a biological
20 effect relevant to a primary treatment, and prophylactic treatments intended to delay, reduce, or prevent the development of a disease or condition, as well as treatments intended to cause the development of a condition different from that which would have been likely to develop in the absence of the treatment.

The term "therapy" refers to a process which is intended to produce a
25 beneficial change in the condition of a mammal, e.g., a human, often referred to as a patient. A beneficial change can, for example, include one or more of: restoration of function, reduction of symptoms, limitation or retardation of progression of a disease, disorder, or condition or prevention, limitation or retardation of deterioration of a patient's condition, disease or disorder. Such therapy can involve,
30 for example, nutritional modifications, administration of radiation, administration of a drug, behavioral modifications, and combinations of these, among others.

The term "drug" as used herein refers to a chemical entity or biological product, or combination of chemical entities or biological products, administered to a person to treat or prevent or control a disease or condition. The chemical entity or
35 biological product is preferably, but not necessarily a low molecular weight compound, but may also be a larger compound, for example, an oligomer of nucleic acids, amino acids, or carbohydrates including without limitation proteins, oligonucleotides, ribozymes, DNazymes, glycoproteins, lipoproteins, and

modifications and combinations thereof. A biological product is preferably a monoclonal or polyclonal antibody or fragment thereof such as a variable chain fragment; cells; or an agent or product arising from recombinant technology, such as, without limitation, a recombinant protein, recombinant vaccine, or DNA construct developed for therapeutic, e.g., human therapeutic, use. The term "drug" may include, without limitation, compounds that are approved for sale as pharmaceutical products by government regulatory agencies (e.g., U.S. Food and Drug Administration (USFDA or FDA), European Medicines Evaluation Agency (EMA), and a world regulatory body governing the International Conference of Harmonization (ICH) rules and guidelines), compounds that do not require approval by government regulatory agencies, food additives or supplements including compounds commonly characterized as vitamins, natural products, and completely or incompletely characterized mixtures of chemical entities including natural compounds or purified or partially purified natural products. The term "drug" as used herein is synonymous with the terms "medicine", "pharmaceutical product", or "product". Most preferably the drug is approved by a government agency for treatment of a specific disease or condition.

A "low molecular weight compound" has a molecular weight $<5,000$ Da, more preferably <2500 Da, still more preferably <1000 Da, and most preferably <700 Da.

Those familiar with drug use in medical practice will recognize that regulatory approval for drug use is commonly limited to approved indications, such as to those patients afflicted with a disease or condition for which the drug has been shown to be likely to produce a beneficial effect in a controlled clinical trial. Unfortunately, it has generally not been possible with current knowledge to predict which patients will have a beneficial response, with the exception of certain diseases such as bacterial infections where suitable laboratory methods have been developed. Likewise, it has generally not been possible to determine in advance whether a drug will be safe in a given patient. Regulatory approval for the use of most drugs is limited to the treatment of selected diseases and conditions. The descriptions of approved drug usage, including the suggested diagnostic studies or monitoring studies, and the allowable parameters of such studies, are commonly described in the "label" or "insert" which is distributed with the drug. Such labels or inserts are preferably required by government agencies as a condition for marketing the drug and are listed in common references such as the Physicians Desk Reference (PDR). These and other limitations or considerations on the use of a drug are also found in medical journals, publications such as pharmacology, pharmacy or medical

textbooks including, without limitation, textbooks of nutrition, allopathic, homeopathic, and osteopathic medicine.

Many widely used drugs are effective in a minority of patients receiving the drug, particularly when one controls for the placebo effect. For example, the PDR shows that about 45% of patients receiving Cognex (tacrine hydrochloride) for Alzheimer's disease show no change or minimal worsening of their disease, as do about 68% of controls (including about 5% of controls who were much worse). About 58% of Alzheimer's patients receiving Cognex were minimally improved, compared to about 33% of controls, while about 2% of patients receiving Cognex were much improved compared to about 1% of controls. Thus a tiny fraction of patients had a significant benefit. Response to treatments for amyotrophic lateral sclerosis are likewise minimal.

Thus, in a first aspect, the invention provides a method for selecting a treatment for a patient suffering from a disease or condition by determining whether or not a gene or genes in cells of the patient (in some cases including both normal and disease cells, such as cancer cells) contain at least one sequence variance which is indicative of the effectiveness of the treatment of the disease or condition. The gene or genes (along with exemplary variances) are specified herein, in Tables 1-6, 12-17, and 18-23. Preferably the at least one variance includes a plurality of variances which may provide a haplotype or haplotypes. Preferably the joint presence of the plurality of variances is indicative of the potential effectiveness or safety of the treatment in a patient having such plurality of variances. The plurality of variances may each be indicative of the potential effectiveness of the treatment, and the effects of the individual variances may be independent or additive, or the plurality of variances may be indicative of the potential effectiveness if at least 2, 3, 4, or more appear jointly. The plurality of variances may also be combinations of these relationships. The plurality of variances may include variances from one, two, three or more gene loci.

In preferred embodiments of aspects of the invention involving genes relating to psychiatric or neurological disease or related conditions or the other diseases or conditions identified herein, or to pharmacological responses to compounds used to treat such diseases or conditions, the gene product is involved in a function as described in the Background of the Invention or otherwise described herein.

In some cases, the selection of a method of treatment, i.e., a therapeutic regimen, may incorporate selection of one or more from a plurality of medical therapies. Thus, the selection may be the selection of a method or methods which is/are more effective or less effective than certain other therapeutic regimens (with

either having varying safety parameters). Likewise or in combination with the preceding selection, the selection may be the selection of a method or methods, which is safer than certain other methods of treatment in the patient.

The selection may involve either positive selection or negative selection or both, meaning that the selection can involve a choice that a particular method would be an appropriate method to use and/or a choice that a particular method would be an inappropriate method to use. Thus, in certain embodiments, the presence of the at least one variance is indicative that the treatment will be effective or otherwise beneficial (or more likely to be beneficial) in the patient. Stating that the treatment will be effective means that the probability of beneficial therapeutic effect is greater than in a person not having the appropriate presence or absence of particular variances. In other embodiments, the presence of the at least one variance is indicative that the treatment will be ineffective or contra-indicated for the patient. For example, a treatment may be contra-indicated if the treatment results, or is more likely to result, in undesirable side effects, or an excessive level of undesirable side effects. A determination of what constitutes excessive side-effects will vary, for example, depending on the disease or condition being treated, the availability of alternatives, the expected or experienced efficacy of the treatment, and the tolerance of the patient. As for an effective treatment, this means that it is more likely that desired effect will result from the treatment administration in a patient with a particular variance or variances than in a patient who has a different variance or variances. Also in preferred embodiments, the presence of the at least one variance is indicative that the treatment is both effective and unlikely to result in undesirable effects or outcomes, or vice versa (is likely to have undesirable side effects but unlikely to produce desired therapeutic effects).

In reference to response to a treatment, the term "tolerance" refers to the ability of a patient to accept a treatment, based, e.g., on deleterious effects and/or effects on lifestyle. Frequently, the term principally concerns the patients perceived magnitude of deleterious effects such as nausea, weakness, dizziness, and diarrhea, among others. Such experienced effects can, for example, be due to general or cell-specific toxicity, activity on non-target cells, cross-reactivity on non-target cellular constituents (non-mechanism based), and/or side effects of activity on the target cellular constituents (mechanism based), or the cause of toxicity may not be understood. In any of these circumstances one may identify an association between the undesirable effects and variances in specific genes.

Adverse responses to drugs constitute a major medical problem, as shown in two recent meta-analyses (Lazarou, J. et al, Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies, JAMA 279:1200-1205,

1998; Bonn, Adverse drug reactions remain a major cause of death, Lancet 351:1183, 1998). An estimated 2.2 million hospitalized patients in the United States had serious adverse drug reactions in 1994, with an estimated 106,000 deaths (Lazarou et al.). To the extent that some of these adverse events are due to
5 genetically encoded biochemical diversity among patients in pathways that effect drug action, the identification of variances that are predictive of such effects will allow for more effective and safer drug use.

In embodiments of this invention, the variance or variant form or forms of a gene is/are associated with a specific response to a drug. The frequency of a specific
10 variance or variant form of the gene may correspond to the frequency of an efficacious response to administration of a drug. Alternatively, the frequency of a specific variance or variant form of the gene may correspond to the frequency of an adverse event resulting from administration of a drug. Alternatively the frequency of a specific variance or variant form of a gene may not correspond closely with the
15 frequency of a beneficial or adverse response, yet the variance may still be useful for identifying a patient subset with high response or toxicity incidence because the variance may account for only a fraction of the patients with high response or toxicity. In such a case the preferred course of action is identification of a second or third or additional variances that permit identification of the patient groups not
20 usefully identified by the first variance. Preferably, the drug will be effective in more than 20% of individuals with one or more specific variances or variant forms of the gene, more preferably in 40% and most preferably in >60%. In other embodiments, the drug will be toxic or create clinically unacceptable side effects in more than 10% of individuals with one or more variances or variant forms of the
25 gene, more preferably in >30%, more preferably in >50%, and most preferably in >70% or in more than 90%.

Also in other embodiments, the method of selecting a treatment includes eliminating or excluding a treatment, where the presence or absence of the at least one variance is indicative that the treatment will be ineffective or contra-indicated,
30 e.g., would result in excessive weight gain. In other preferred embodiments, in cases in which undesirable side-effects may occur or are expected to occur from a particular therapeutic treatment, the selection of a method of treatment can include identifying both a first and second treatment, where the first treatment is effective to treat the disease or condition, and the second treatment reduces a deleterious effect
35 or enhance efficacy of the first treatment.

The phrase "eliminating a treatment" (similarly for excluding a treatment) refers to removing a possible treatment from consideration, e.g., for use with a particular patient based on the presence or absence of a particular variance(s) in one

or more genes in cells of that patient, or to stopping the administration of a treatment.

Usually, the treatment will involve the administration of a compound preferentially active or safe in patients with a form or forms of a gene, where the gene is one identified herein. The administration may involve a combination of compounds. Thus, in preferred embodiments, the method involves identifying such an active compound or combination of compounds, where the compound is less active or is less safe or both when administered to a patient having a different form of the gene.

Also in preferred embodiments, the method of selecting a treatment involves selecting a method of administration of a compound, combination of compounds, or pharmaceutical composition, for example, selecting a suitable dosage level and/or frequency of administration, and/or mode of administration of a compound. The method of administration can be selected to provide better, preferably maximum therapeutic benefit. In this context, "maximum" refers to an approximate local maximum based on the parameters being considered, not an absolute maximum.

Also in this context, a "suitable dosage level" refers to a dosage level which provides a therapeutically reasonable balance between pharmacological effectiveness and deleterious effects. Often this dosage level is related to the peak or average serum levels resulting from administration of a drug at the particular dosage level.

Similarly, a "frequency of administration" refers to how often in a specified time period a treatment is administered, e.g., once, twice, or three times per day, every other day, once per week, etc. For a drug or drugs, the frequency of administration is generally selected to achieve a pharmacologically effective average or peak serum level without excessive deleterious effects (and preferably while still being able to have reasonable patient compliance for self-administered drugs). Thus, it is desirable to maintain the serum level of the drug within a therapeutic window of concentrations for the greatest percentage of time possible without such deleterious effects as would cause a prudent physician to reduce the frequency of administration for a particular dosage level.

A particular gene or genes can be relevant to the treatment of more than one disease or condition, for example, the gene or genes can have a role in the initiation, development, course, treatment, treatment outcomes, or health-related quality of life outcomes of a number of different diseases, disorders, or conditions. Thus, in preferred embodiments, the disease or condition or treatment of the disease or condition is any which involves a gene from the gene list described herein as Tables 1-6, 12-17, and 18-23.

Determining the presence of a particular variance or plurality of variances in a particular gene in a patient can be performed in a variety of ways. In preferred embodiments, the detection of the presence or absence of at least one variance involves amplifying a segment of nucleic acid including at least one of the at least one variances. Preferably a segment of nucleic acid to be amplified is 500 nucleotides or less in length, more preferably 100 nucleotides or less, and most preferably 45 nucleotides or less. Also, preferably the amplified segment or segments includes a plurality of variances, or a plurality of segments of a gene or of a plurality of genes. In other embodiments, e.g., where a haplotype is to be determined, the segment of nucleic acid is at least 500 nucleotides in length, or at least 2 kb in length, or at least 5 kb in length.

In preferred embodiments, determining the presence of a set of variances in a specific gene related to treatment of disease, disorders, or dysfunctions or other related genes, or genes listed in Tables 1-6, 12-17, and 18-23, includes a haplotyping test that requires allele specific amplification of a large DNA segment of no greater than 25,000 nucleotides, preferably no greater than 10,000 nucleotides and most preferably no greater than 5,000 nucleotides. Alternatively one allele may be enriched by methods other than amplification prior to determining genotypes at specific variant positions on the enriched allele as a way of determining haplotypes. Preferably the determination of the presence or absence of a haplotype involves determining the sequence of the variant sites by methods such as chain terminating DNA sequencing or minisequencing, or by oligonucleotide hybridization or by mass spectrometry. For the use of mass spectrometry, the method can involve detection of the mass of a fragment or fragments and can further involve inferring the genotype (e.g., the specific variance at a site) from the masses determined.

The term "genotype" in the context of this invention refers to the alleles present in DNA from a subject or patient, where an allele can be defined by the particular nucleotide(s) present in a nucleic acid sequence at a particular site(s). Often a genotype is the nucleotide(s) present at a single polymorphic site known to vary in the human population.

In preferred embodiments, the detection of the presence or absence of the at least one variance involves contacting a nucleic acid sequence corresponding to one of the genes identified above or a product of such a gene with a probe. The probe is able to distinguish a particular form of the gene or gene product or the presence or a particular variance or variances, e.g., by differential binding or hybridization. Thus, exemplary probes include nucleic acid hybridization probes, peptide nucleic acid probes, nucleotide-containing probes which also contain at least one nucleotide analog, and antibodies, e.g., monoclonal antibodies, and other probes as discussed

herein. Those skilled in the art are familiar with the preparation of probes with particular specificities. Those skilled in the art will recognize that a variety of variables can be adjusted to optimize the discrimination between two variant forms of a gene, including changes in salt concentration, temperature, pH and addition of various compounds that affect the differential affinity of GC vs. AT base pairs, such as tetramethyl ammonium chloride. (See Current Protocols in Molecular Biology by F.M. Ausubel, R. Brent, R.E. Kingston, D.D. Moore, J.D. Seidman, K. Struhl, and V.B. Chanda (editors, John Wiley & Sons.)

In other preferred embodiments, determining the presence or absence of the at least one variance involves sequencing at least one nucleic acid sample. The sequencing involves sequencing of a portion or portions of a gene and/or portions of a plurality of genes which includes at least one variance site, and may include a plurality of such sites. Preferably, the portion is 500 nucleotides or less in length, more preferably 100 nucleotides or less, and most preferably 45 nucleotides or less in length. Such sequencing can be carried out by various methods recognized by those skilled in the art, including use of dideoxy termination methods (e.g., using dye-labeled dideoxy nucleotides) and the use of mass spectrometric methods. In addition, mass spectrometric methods may be used to determine the nucleotide present at a variance site. In preferred embodiments in which a plurality of variances is determined, the plurality of variances can constitute a haplotype or collection of haplotypes. Preferably the methods for determining genotypes or haplotypes are designed to be sensitive to all the common genotypes or haplotypes present in the population being studied (for example, a clinical trial population).

The terms "variant form of a gene", "form of a gene", or "allele" refer to one specific form of a gene in a population, the specific form differing from other forms of the same gene in the sequence of at least one, and frequently more than one, variant sites within the sequence of the gene. The sequences at these variant sites that differ between different alleles of the gene are termed "gene sequence variances" or "variances" or "variants". The term "alternative form" refers to an allele that can be distinguished from other alleles by having distinct variances at least one, and frequently more than one, variant sites within the gene sequence. Other terms known in the art to be equivalent include mutation and polymorphism, although mutation is often used to refer to an allele associated with a deleterious phenotype. In preferred aspects of this invention, the variances are selected from the group consisting of the variances listed in the variance tables herein or in a patent or patent application referenced and incorporated by reference in this disclosure. In the methods utilizing variance presence or absence, reference to the presence of a variance or variances means particular variances, i.e., particular nucleotides at

particular polymorphic sites, rather than just the presence of any variance in the gene.

Variances occur in the human genome at approximately one in every 500 – 1,000 bases within the human genome when two alleles are compared. When multiple alleles from unrelated individuals are compared the density of variant sites increases as different individuals, when compared to a reference sequence, will often have sequence variances at different sites. At most variant sites there are only two alternative nucleotides involving the substitution of one base for another or the insertion/deletion of one or more nucleotides. Within a gene there may be several variant sites. Variant forms of the gene or alternative alleles can be distinguished by the presence of alternative variances at a single variant site, or a combination of several different variances at different sites (haplotypes).

It is estimated that there are 3,300,000,000 bases in the sequence of a single haploid human genome. All human cells except germ cells are normally diploid. Each gene in the genome may span 100-10,000,000 bases of DNA sequence or 100-20,000 bases of mRNA. It is estimated that there are between 60,000 and 150,000 genes in the human genome. The "identification" of genetic variances or variant forms of a gene involves the discovery of variances that are present in a population. The identification of variances is required for development of a diagnostic test to determine whether a patient has a variant form of a gene that is known to be associated with a disease, condition, or predisposition or with the efficacy or safety of the drug. Identification of previously undiscovered genetic variances is distinct from the process of "determining" the status of known variances by a diagnostic test (often referred to as genotyping). The present invention provides exemplary variances in genes listed in the gene tables, as well as methods for discovering additional variances in those genes and a comprehensive written description of such additional possible variances. Also described are methods for DNA diagnostic tests to determine the DNA sequence at a particular variant site or sites.

The process of "identifying" or discovering new variances involves comparing the sequence of at least two alleles of a gene, more preferably at least 10 alleles and most preferably at least 50 alleles (keeping in mind that each somatic cell has two alleles). The analysis of large numbers of individuals to discover variances in the gene sequence between individuals in a population will result in detection of a greater fraction of all the variances in the population. Preferably the process of identifying reveals whether there is a variance within the gene; more preferably identifying reveals the location of the variance within the gene; more preferably identifying provides knowledge of the sequence of the nucleic acid sequence of the

variance, and most preferably identifying provides knowledge of the combination of different variances that comprise specific variant forms of the gene (referred to as alleles). In identifying new variances it is often useful to screen different population groups based on racial, ethnic, gender, and/or geographic origin because particular
5 variances may differ in frequency between such groups. It may also be useful to screen DNA from individuals with a particular disease or condition of interest because they may have a higher frequency of certain variances than the general population.

The process of genotyping involves using diagnostic tests for specific
10 variances that have already been identified. It will be apparent that such diagnostic tests can only be performed after variances and variant forms of the gene have been identified. Identification of new variances can be accomplished by a variety of methods, alone or in combination, including, for example, DNA sequencing, SSCP, heteroduplex analysis, denaturing gradient gel electrophoresis (DGGE),
15 heteroduplex cleavage (either enzymatic as with T4 Endonuclease 7, or chemical as with osmium tetroxide and hydroxylamine), computational methods (described herein), and other methods described herein as well as others known to those skilled in the art. (See, for example: Cotton, R.G.H., Slowly but surely towards better scanning for mutations, Trends in Genetics 13(2): 43-6, 1997 or Current Protocols in
20 Human Genetics by N.C. Dracoli, J.L. Haines, B.R. Korf, D.T. Moir, C.C. Morton, C.E. Seidman, D.R. Smith, and A. Boyle (editors), John Wiley & Sons.)

In the context of this invention, the term "analyzing a sequence" refers to determining at least some sequence information about the sequence, e.g., determining the nucleotides present at a particular site or sites in the sequence,
25 particularly sites that are known to vary in a population, or determining the base sequence of all or of a portion of the particular sequence.

In the context of this invention, the term "haplotype" refers to a *cis* arrangement of two or more polymorphic nucleotides, i.e., variances, on a particular chromosome, e.g., in a particular gene. The haplotype preserves information about
30 the phase of the polymorphic nucleotides – that is, which set of variances were inherited from one parent, and which from the other. A genotyping test does not provide information about phase. For example, an individual heterozygous at nucleotide 25 of a gene (both A and C are present) and also at nucleotide 100 (both G and T are present) could have haplotypes 25A – 100G and 25C – 100T, or
35 alternatively 25A – 100T and 25C – 100G. Only a haplotyping test can discriminate these two cases definitively.

The terms "variances", "variants" and "polymorphisms", as used herein, may also refer to a set of variances, haplotypes or a mixture of the two, unless otherwise

indicated. Further, the term variance, variant or polymorphism (singular), as used herein, also encompasses a haplotype unless otherwise indicated. This usage is intended to minimize the need for cumbersome phrases such as: "...measure correlation between drug response and *a variance, variances, haplotype, haplotypes or a combination of variances and haplotypes...*", throughout the application.

Instead, the italicized text in the foregoing sentence can be represented by the word "variance", "variant" or "polymorphism". Similarly, the term genotype, as used herein, means a procedure for determining the status of one or more variances in a gene, including a set of variances comprising a haplotype. Thus phrases such as "...genotype a patient..." refer to determining the status of one or more variances, including a set of variances for which phase is known (i.e. a haplotype).

In preferred embodiments of this invention, the frequency of the variance or variant form of the gene in a population is known. Measures of frequency known in the art include "allele frequency", namely the fraction of genes in a population that have one specific variance or set of variances. The allele frequencies for any gene should sum to 1. Another measure of frequency known in the art is the "heterozygote frequency" namely, the fraction of individuals in a population who carry two alleles, or two forms of a particular variance or variant form of a gene, one inherited from each parent. Alternatively, the number of individuals who are homozygous for a particular form of a gene may be a useful measure. The relationship between allele frequency, heterozygote frequency, and homozygote frequency is described for many genes by the Hardy-Weinberg equation, which provides the relationship between allele frequency, heterozygote frequency and homozygote frequency in a freely breeding population at equilibrium. Most human variances are substantially in Hardy-Weinberg equilibrium. In a preferred aspect of this invention, the allele frequency, heterozygote frequency, and homozygote frequencies are determined experimentally. Preferably a variance has an allele frequency of at least 0.01, more preferably at least 0.05, still more preferably at least 0.10. However, the allele may have a frequency as low as 0.001 if the associated phenotype is, for example, a rare form of toxic reaction to a treatment or drug. Beneficial responses may also be rare.

In this regard, "population" refers to a defined group of individuals or a group of individuals with a particular disease or condition or individuals that may be treated with a specific drug identified by, but not limited to geographic, ethnic, race, gender, and/or cultural indices. In most cases a population will preferably encompass at least ten thousand, one hundred thousand, one million, ten million, or more individuals, with the larger numbers being more preferable. In preferred embodiments of this invention, the population refers to individuals with a specific

disease or condition that may be treated with a specific drug. In embodiments of this invention, the allele frequency, heterozygote frequency, or homozygote frequency of a specific variance or variant form of a gene is known. In preferred embodiments of this invention, the frequency of one or more variances that may predict response to a treatment is determined in one or more populations using a diagnostic test.

It should be emphasized that it is currently not generally practical to study an entire population to establish the association between a specific disease or condition or response to a treatment and a specific variance or variant form of a gene. Such studies are preferably performed in controlled clinical trials using a limited number of patients that are considered to be representative of the population with the disease. Since drug development programs are generally targeted at the largest possible population, the study population will generally consist of men and women, as well as members of various racial and ethnic groups, depending on where the clinical trial is being performed. This is important to establish the efficacy of the treatment in all segments of the population.

In the context of this invention, the term "probe" refers to a molecule that detectably distinguishes between target molecules differing in structure. Detection can be accomplished in a variety of different ways depending on the type of probe used and the type of target molecule. Thus, for example, detection may be based on discrimination of activity levels of the target molecule, but preferably is based on detection of specific binding. Examples of such specific binding include antibody binding and nucleic acid probe hybridization. Thus, for example, probes can include enzyme substrates, antibodies and antibody fragments, and nucleic acid hybridization probes. Thus, in preferred embodiments, the detection of the presence or absence of the at least one variance involves contacting a nucleic acid sequence which includes a variance site with a probe, preferably a nucleic acid probe, where the probe preferentially hybridizes with a form of the nucleic acid sequence containing a complementary base at the variance site as compared to hybridization to a form of the nucleic acid sequence having a non-complementary base at the variance site, where the hybridization is carried out under selective hybridization conditions. Such a nucleic acid hybridization probe may span two or more variance sites. Unless otherwise specified, a nucleic acid probe can include one or more nucleic acid analogs, labels or other substituents or moieties so long as the base-pairing function is retained.

As is generally understood, administration of a particular treatment, e.g., administration of a therapeutic compound or combination of compounds, is chosen depending on the disease or condition that is to be treated. Thus, in certain preferred

embodiments, the disease or condition is one for which administration of a treatment is expected to provide a therapeutic benefit; in certain embodiments, the compound is a compound identified herein, e.g., in a drug table (Tables 24-68).

As used herein, the terms "effective" and "effectiveness" includes both pharmacological effectiveness and physiological safety. Pharmacological effectiveness refers to the ability of the treatment to result in a desired biological effect in the patient. Physiological safety refers to the level of toxicity, or other adverse physiological effects at the cellular, organ and/or organism level (often referred to as side-effects) resulting from administration of the treatment. On the other hand, the term "ineffective" indicates that a treatment does not provide sufficient pharmacological effect to be therapeutically useful, even in the absence of deleterious effects, at least in the unstratified population. (Such a treatment may be ineffective in a subgroup that can be identified by the presence of one or more sequence variances or alleles.) "Less effective" means that the treatment results in a therapeutically significant lower level of pharmacological effectiveness and/or a therapeutically greater level of adverse physiological effects, e.g., greater liver toxicity.

Thus, in connection with the administration of a drug, a drug which is "effective against" a disease or condition indicates that administration in a clinically appropriate manner results in a beneficial effect for at least a statistically significant fraction of patients, such as a improvement of symptoms, a cure, a reduction in disease load, reduction in tumor mass or cell numbers, extension of life, improvement in quality of life, or other effect generally recognized as positive by medical doctors familiar with treating the particular type of disease or condition.

Effectiveness is measured in a particular population. In conventional drug development the population is generally every subject who meets the enrollment criteria (i.e. has the particular form of the disease or condition being treated). It is an aspect of the present invention that segmentation of a study population by genetic criteria can provide the basis for identifying a subpopulation in which a drug is effective against the disease or condition being treated.

The term "deleterious effects" refers to physical effects in a patient caused by administration of a treatment which are regarded as medically undesirable. Thus, for example, deleterious effects can include a wide spectrum of toxic effects injurious to health such as death of normally functioning cells when only death of diseased cells is desired, nausea, fever, inability to retain food, dehydration, damage to critical organs such as arrhythmias, renal tubular necrosis, fatty liver, or pulmonary fibrosis leading to coronary, renal, hepatic, or pulmonary insufficiency among many others. In this regard, the term "contra-indicated" means that a treatment results in

deleterious effects such that a prudent medical doctor treating such a patient would regard the treatment as unsuitable for administration. Major factors in such a determination can include, for example, availability and relative advantages of alternative treatments, consequences of non-treatment, and permanency of deleterious effects of the treatment.

It is recognized that many treatment methods, e.g., administration of certain compounds or combinations of compounds, may produce side-effects or other deleterious effects in patients. Such effects can limit or even preclude use of the treatment method in particular patients, or may even result in irreversible injury, dysfunction, or death of the patient. Thus, in certain embodiments, the variance information is used to select both a first method of treatment and a second method of treatment. Usually the first treatment is a primary treatment which provides a physiological effect directed against the disease or condition or its symptoms. The second method is directed to reducing or eliminating one or more deleterious effects or enhancing efficacy of the first treatment, e.g., to reduce a general toxicity or to reduce a side effect of the primary treatment. Thus, for example, the second method can be used to allow use of a greater dose or duration of the first treatment, or to allow use of the first treatment in patients for whom the first treatment would not be tolerated or would be contra-indicated in the absence of a second method to reduce deleterious effects or to potentiate the effectiveness of the first treatment.

In a related aspect, the invention concerns a method for providing a correlation between a patient genotype and effectiveness of a treatment, by determining the presence or absence of a particular known variance or variances in cells of a patient for a gene from Tables 1-6, 12-17, and 18-23, or other gene related to neurological disease or other disease identified herein, and providing a result indicating the expected effectiveness of a treatment for a disease or condition. The result may be formulated by comparing the genotype of the patient with a list of variances indicative of the effectiveness of a treatment, e.g., administration of a drug described herein. The determination may be by methods as described herein or other methods known to those skilled in the art.

In a related aspect, the invention provides a method for selecting a method of treatment for a patient suffering from a disease or condition as identified herein by comparing at least one variance in at least one gene in the patient, with a list of variances in the gene from Tables 1-6, 12-17, and 18-23, or other gene related to a disease or condition listed herein, which are indicative of the effectiveness of at least one method of treatment. Preferably the comparison involves a plurality of variances or a haplotype indicative of the effectiveness of at least one method of treatment. Also, preferably the list of variances includes a plurality of variances.

Similar to the above aspect, in preferred embodiments the at least one method of treatment involves the administration of a compound effective in at least some patients with a disease or condition; the presence or absence of the at least one variance is indicative that the treatment will be effective in the patient; and/or the presence or absence of the at least one variance is indicative that the treatment will be ineffective or contra-indicated in the patient; and/or the treatment is a first treatment and the presence or absence of the at least one variance is indicative that a second treatment will be beneficial to reduce a deleterious effect of or potentiate the effectiveness of the first treatment; and/or the at least one treatment is a plurality of methods of treatment. For a plurality of treatments, preferably the selecting involves determining whether any of the methods of treatment will be more effective than at least one other of the plurality of methods of treatment. Yet other embodiments are provided as described for the preceding aspect in connection with methods of treatment using administration of a compound; treatment of various diseases, and variances in particular genes.

In the context of variance information in the methods of this invention, the term "list" refers to one or more, preferably at least 2, 3, 4, 5, 7, or 10 variances that have been identified for a gene of potential importance in accounting for inter-individual variation in treatment response. Preferably there is a plurality of variances for the gene, preferably a plurality of variances for the particular gene. Preferably, the list is recorded in written or electronic form. For example, identified variances of identified genes are recorded for some of the genes in Tables 12-17 and 18-23; additional variances for genes in Tables 1-6 can be readily identified by one skilled in the art using any of a variety of methods. The list may also contain haplotypes, either alone or with other variances.

In addition to the basic method of treatment, often the mode of administration of a given compound as a treatment for a disease or condition in a patient is significant in determining the course and/or outcome of the treatment for the patient. Thus, the invention also provides a method for selecting a method of administration of a compound to a patient suffering from a disease or condition, by determining the presence or absence of at least one variance in cells of the patient in at least one identified gene from Tables 1-6, 12-17, and 18-23, where such presence or absence is indicative of an appropriate method of administration of the compound. Preferably, the selection of a method of treatment (a treatment regimen) involves selecting a dosage level or frequency of administration or route of administration of the compound or combinations of those parameters. In preferred embodiments, two or more compounds are to be administered, and the selecting involves selecting a method of administration for one, two, or more than two of the

compounds, jointly, concurrently, or separately. As understood by those skilled in the art, such plurality of compounds may be used in combination therapy, and thus may be formulated in a single drug, or may be separate drugs administered concurrently, serially, or separately. Other embodiments are as indicated above for selection of second treatment methods, methods of identifying variances, and methods of treatment as described for aspects above.

In another aspect, the invention provides a method for selecting a patient for administration of a method of treatment for a disease or condition, or of selecting a patient for a method of administration of a treatment, by comparing the presence or absence of at least one variance in a gene as identified above in cells of a patient, with a list of variances in the gene, where the presence or absence of the at least one variance is indicative that the treatment or method of administration will be effective in the patient. If the at least one variance is present in the patient's cells, then the patient is selected for administration of the treatment.

In preferred embodiments, the disease or the method of treatment is as described in aspects above, specifically including, for example, those described for selecting a method of treatment.

In another aspect, the invention provides a method for identifying a subset of patients with enhanced or diminished response or tolerance to a treatment method or a method of administration of a treatment where the treatment is for a disease or condition in the patient. The method involves correlating one or more variances in one or more genes as identified in aspects above in a plurality of patients with response to a treatment or a method of administration of a treatment. The correlation may be performed by determining the one or more variances in the one or more genes in the plurality of patients and correlating the presence or absence of each of the variances (alone or in various combinations) with the patient's response to treatment. The variances may be previously known to exist or may also be determined in the present method or combinations of prior information and newly determined information may be used. The enhanced or diminished response should be statistically significant, preferably such that $p = 0.10$ or less, more preferably 0.05 or less, and most preferably 0.02 or less. A positive correlation between the presence of one or more variances and an enhanced response to treatment is indicative that the treatment is particularly effective in the group of patients having those variances. A positive correlation of the presence of the one or more variances with a diminished response to the treatment is indicative that the treatment will be less effective in the group of patients having those variances. Such information is useful, for example, for selecting or de-selecting patients for a particular treatment or method of administration of a treatment, or for demonstrating that a group of

patients exists for which the treatment or method of treatment would be particularly beneficial or contra-indicated. Such demonstration can be beneficial, for example, for obtaining government regulatory approval for a new drug or a new use of a drug

5 In preferred embodiments, the variances are in at least one of the identified genes listed on Tables 1-6, 12-17, and 18-23, or are particular variances described herein. Also, preferred embodiments include drugs, treatments, variance identification or determination, determination of effectiveness, and/or diseases as described for aspects above or otherwise described herein.

10 In preferred embodiments, the correlation of patient responses to therapy according to patient genotype is carried out in a clinical trial, e.g., as described herein according to any of the variations described. Detailed description of methods for associating variances with clinical outcomes using clinical trials are provided below. Further, in preferred embodiments the correlation of pharmacological effect (positive or negative) to treatment response according to genotype or haplotype in
15 such a clinical trial is part of a regulatory submission to a government agency leading to approval of the drug. Most preferably the compound or compounds would not be approvable in the absence of the genetic information allowing identification of an optimal responder population.

20 As indicated above, in aspects of this invention involving selection of a patient for a treatment, selection of a method or mode of administration of a treatment, and selection of a patient for a treatment or a method of treatment, the selection may be positive selection or negative selection. Thus, the methods can include eliminating or excluding a treatment for a patient, eliminating or excluding a method or mode of administration of a treatment to a patient, or elimination or
25 exclusion of a patient for a treatment or method of treatment.

Also, in methods involving identification and/or comparison of variances present in a gene of a patient, the methods can involve such identification or comparison for a plurality of genes. Preferably, the genes are functionally related to the same disease or condition, or to the aspect of disease pathophysiology that is
30 being subjected to pharmacological manipulation by the treatment (e.g., a drug), or to the activation or inactivation or elimination of the drug, and more preferably the genes are involved in the same biochemical process or pathway.

35 In another aspect, the invention provides a method for identifying the forms of a gene in an individual, where the gene is one specified as for aspects above, by determining the presence or absence of at least one variance in the gene. In preferred embodiments, the at least one variance includes at least one variance selected from the group of variances identified in variance tables herein. Preferably, the presence or absence of the at least one variance is indicative of the effectiveness

of a therapeutic treatment in a patient suffering from a disease or condition and having cells containing the at least one variance.

The presence or absence of the variances can be determined in any of a variety of ways as recognized by those skilled in the art. For example, the
5 nucleotide sequence of at least one nucleic acid sequence which includes at least one variance site (or a complementary sequence) can be determined, such as by chain termination methods, hybridization methods or by mass spectrometric methods. Likewise, in preferred embodiments, the determining involves contacting a nucleic acid sequence or a gene product of one of one of the genes with a probe that
10 specifically identifies the presence or absence of a form of the gene. For example, a probe, e.g., a nucleic acid probe, can be used which specifically binds, e.g., hybridizes, to a nucleic acid sequence corresponding to a portion of the gene and which includes at least one variance site under selective binding conditions. As described for other aspects, determining the presence or absence of at least two
15 variances and their relationship on the two gene copies present in a patient can constitute determining a haplotype or haplotypes.

Other preferred embodiments involve variances related to types of treatment, drug responses, diseases, nucleic acid sequences, and other items related to variances and variance determination as described for aspects above.

20 In yet another aspect, the invention provides a pharmaceutical composition which includes a compound which has a differential effect in patients having at least one copy, or alternatively, two copies of a form of a gene as identified for aspects above and a pharmaceutically acceptable carrier, excipient, or diluent. The composition is adapted to be preferentially effective to treat a patient with cells
25 containing the one, two, or more copies of the form of the gene.

In preferred embodiments of aspects involving pharmaceutical compositions, active compounds, or drugs, the material is subject to a regulatory limitation or restriction on approved uses or indications, e.g., by the U.S. Food and Drug Administration (FDA), limiting approved use of the composition to patients having
30 at least one copy of the particular form of the gene which contains at least one variance. Alternatively, the composition is subject to a regulatory limitation or restriction on approved uses indicating that the composition is not approved for use or should not be used in patients having at least one copy of a form of the gene including at least one variance. Also in preferred embodiments, the composition is
35 packaged, and the packaging includes a label or insert indicating or suggesting beneficial therapeutic approved use of the composition in patients having one or two copies of a form of the gene including at least one variance. Alternatively, the label or insert limits approved use of the composition to patients having zero or one

or two copies of a form of the gene including at least one variance. The latter embodiment would be likely where the presence of the at least one variance in one or two copies in cells of a patient means that the composition would be ineffective or deleterious to the patient. Also in preferred embodiments, the composition is indicated for use in treatment of a disease or condition which is one of those identified for aspects above. Also in preferred embodiments, the at least one variance includes at least one variance from those identified herein.

The term "packaged" means that the drug, compound, or composition is prepared in a manner suitable for distribution or shipping with a box, vial, pouch, bubble pack, or other protective container, which may also be used in combination. The packaging may have printing on it and/or printed material may be included in the packaging.

In preferred embodiments, the drug is selected from the drug classes or specific exemplary drugs identified in an example, in a table herein, and is subject to a regulatory limitation or suggestion or warning as described above that limits or suggests limiting approved use to patients having specific variances or variant forms of a gene identified in Examples or in the gene list provided below in order to achieve maximal benefit and avoid toxicity or other deleterious effect.

A pharmaceutical composition can be adapted to be preferentially effective in a variety of ways. In some cases, an active compound is selected which was not previously known to be differentially active, or which was not previously recognized as a potential therapeutic compound. In some cases, the concentration of an active compound which has differential activity can be adjusted such that the composition is appropriate for administration to a patient with the specified variances. For example, the presence of a specified variance may allow or require the administration of a much larger dose, which would not be practical with a previously utilized composition. Conversely, a patient may require a much lower dose, such that administration of such a dose with a prior composition would be impractical or inaccurate. Thus, the composition may be prepared in a higher or lower unit dose form, or prepared in a higher or lower concentration of the active compound or compounds. In yet other cases, the composition can include additional compounds needed to enable administration of a particular active compound in a patient with the specified variances, which was not in previous compositions, e.g., because the majority of patients did not require or benefit from the added component.

The term "differential" or "differentially" generally refers to a statistically significant different level in the specified property or effect. Preferably, the difference is also functionally significant. Thus, "differential binding or hybridization" is sufficient difference in binding or hybridization to allow

discrimination using an appropriate detection technique. Likewise, "differential effect" or "differentially active" in connection with a therapeutic treatment or drug refers to a difference in the level of the effect or activity which is distinguishable using relevant parameters and techniques for measuring the effect or activity being considered. Preferably the difference in effect or activity is also sufficient to be clinically significant, such that a corresponding difference in the course of treatment or treatment outcome would be expected, at least on a statistical basis.

Also usefully provided in the present invention are probes which specifically recognize a nucleic acid sequence corresponding to a variance or variances in a gene as identified in aspects above or a product expressed from the gene, and are able to distinguish a variant form of the sequence or gene or gene product from one or more other variant forms of that sequence, gene, or gene product under selective conditions. Those skilled in the art recognize and understand the identification or determination of selective conditions for particular probes or types of probes. An exemplary type of probe is a nucleic acid hybridization probe, which will selectively bind under selective binding conditions to a nucleic acid sequence or a gene product corresponding to one of the genes identified for aspects above. Another type of probe is a peptide or protein, e.g., an antibody or antibody fragment which specifically or preferentially binds to a polypeptide expressed from a particular form of a gene as characterized by the presence or absence of at least one variance. Thus, in another aspect, the invention concerns such probes. In the context of this invention, a "probe" is a molecule, commonly a nucleic acid, though also potentially a protein, carbohydrate, polymer, or small molecule, that is capable of binding to one variance or variant form of the gene to a greater extent than to a form of the gene having a different base at one or more variance sites, such that the presence of the variance or variant form of the gene can be determined. Preferably the probe distinguishes at least one variance identified in Examples, tables or lists below or is a variance otherwise identified in a gene identified herein.

In preferred embodiments, the probe is a nucleic acid probe at least 15, preferably at least 17 nucleotides in length, more preferably at least 20 or 22 or 25, preferably 500 or fewer nucleotides in length, more preferably 200 or 100 or fewer, still more preferably 50 or fewer, and most preferably 30 or fewer. In preferred embodiments, the probe has a length in a range between from any one of the above lengths to any other of the above lengths (including endpoints). In the case of certain types of probes, e.g., peptide nucleic acid probes, the probe may be shorter, e.g., 6, 7, 8, 10, or 12 nucleotides in length. The probe specifically hybridizes under selective hybridization conditions to a nucleic acid sequence corresponding to a portion of one of the genes identified in connection with above aspects. The nucleic

acid sequence includes at least one variance site. Also in preferred embodiments, the probe has a detectable label, preferably a fluorescent label. A variety of other detectable labels are known to those skilled in the art. Such a nucleic acid probe can also include one or more nucleic acid analogs.

5 In preferred embodiments, the probe is an antibody or antibody fragment which specifically binds to a gene product expressed from a form of one of the above genes, where the form of the gene has at least one specific variance with a particular base at the variance site, and preferably a plurality of such variances.

10 In connection with nucleic acid probe hybridization, the term "specifically hybridizes" indicates that the probe hybridizes to a sufficiently greater degree to the target sequence than to a sequence having a mismatched base at least one variance site to allow distinguishing such hybridization. The term "specifically hybridizes" thus means that the probe hybridizes to the target sequence, and not to non-target sequences, at a level which allows ready identification of probe/target sequence
15 hybridization under selective hybridization conditions. Thus, "selective hybridization conditions" refer to conditions which allow such differential binding. Similarly, the terms "specifically binds" and "selective binding conditions" refer to such differential binding of any type of probe, e.g., antibody probes, and to the conditions which allow such differential binding. Typically hybridization reactions
20 to determine the status of variant sites in patient samples are carried out with two different probes, one specific for each of the (usually two) possible variant nucleotides. The complementary information derived from the two separate hybridization reactions is useful in corroborating the results.

25 Likewise, the invention provides an isolated, purified or enriched nucleic acid sequence of 15 to 500 nucleotides in length, preferably 15 to 100 nucleotides in length, more preferably 15 to 50 nucleotides in length, and most preferably 15 to 30 nucleotides in length, which has a sequence which corresponds to a portion of one of the genes identified for aspects above. Preferably the lower limit for the preceding ranges is 17, 20, 22, or 25 nucleotides in length. In other embodiments, the nucleic
30 acid sequence is 30 to 300 nucleotides in length, or 45 to 200 nucleotides in length, or 45 to 100 nucleotides in length. The nucleic acid sequence includes at least one variance site. Such sequences can, for example, be amplification products of a sequence which spans or includes a variance site in a gene identified herein. Likewise, such a sequence can be a primer that is able to bind to or extend through a
35 variance site in such a gene. Yet another example is a nucleic acid hybridization probe comprised of such a sequence. In such probes, primers, and amplification products, the nucleotide sequence can contain a sequence or site corresponding to a variance site or sites, for example, a variance site identified herein. Preferably the

presence or absence of a particular variant form in the heterozygous or homozygous state is indicative of the effectiveness of a method of treatment in a patient.

In reference to nucleic acid sequences which "correspond" to a gene, the term "correspond" refers to a nucleotide sequence relationship, such that the
5 nucleotide sequence has a nucleotide sequence which is the same as the reference gene or an indicated portion thereof, or has a nucleotide sequence which is exactly complementary in normal Watson-Crick base pairing, or is an RNA equivalent of such a sequence, e.g., an mRNA, or is a cDNA derived from an mRNA of the gene.

In another aspect, the invention provides a method for determining a
10 genotype of an individual in relation to one or more variances in one or more of the genes identified in above aspects by using mass spectrometric determination of a nucleic acid sequence which is a portion of a gene identified for other aspects of this invention or a complementary sequence. Such mass spectrometric methods are known to those skilled in the art. In preferred embodiments, the method involves
15 determining the presence or absence of a variance in a gene; determining the nucleotide sequence of the nucleic acid sequence; the nucleotide sequence is 100 nucleotides or less in length, preferably 50 or less, more preferably 30 or less, and still more preferably 20 nucleotides or less. In general, such a nucleotide sequence includes at least one variance site, preferably a variance site which is informative
20 with respect to the expected response of a patient to a treatment as described for above aspects.

As indicated above, many therapeutic compounds or combinations of compounds or pharmaceutical compositions show variable efficacy and/or safety in various patients in whom the compound or compounds is administered. Thus, it is
25 beneficial to identify variances in relevant genes, e.g., genes related to the action or toxicity of the compound or compounds. Thus, in a further aspect, the invention provides a method for determining whether a compound has a differential effect due to the presence or absence of at least one variance in a gene or a variant form of a gene, where the gene is a gene identified for aspects above.

The method involves identifying a first patient or set of patients suffering
30 from a disease or condition whose response to a treatment differs from the response (to the same treatment) of a second patient or set of patients suffering from the same disease or condition, and then determining whether the occurrence or frequency of occurrence of at least one variance in at least one gene differs between the first
35 patient or set of patients and the second patient or set of patients. A correlation or other appropriate statistical test between the presence or absence of the variance or variances and the response of the patient or patients to the treatment indicates that the variance provides information about variable patient response. In general, the

method will involve identifying at least one variance in at least one gene. An alternative approach is to identify a first patient or set of patients suffering from a disease or condition and having a particular genotype, haplotype or combination of genotypes or haplotypes, and a second patient or set of patients suffering from the same disease or condition that have a genotype or haplotype or sets of genotypes or haplotypes that differ in a specific way from those of the first set of patients.

Subsequently the extent and magnitude of clinical response can be compared between the first patient or set of patients and the second patient or set of patients. A correlation between the presence or absence of a variance or variances or haplotypes and the response of the patient or patients to the treatment indicates that the variance provides information about variable patient response and is useful for the present invention.

The method can utilize a variety of different informative comparisons to identify correlations. For example a plurality of pairwise comparisons of treatment response and the presence or absence of at least one variance can be performed for a plurality of patients. Likewise, the method can involve comparing the response of at least one patient homozygous for at least one variance with at least one patient homozygous for the alternative form of that variance or variances. The method can also involve comparing the response of at least one patient heterozygous for at least one variance with the response of at least one patient homozygous for the at least one variance. Preferably the heterozygous patient response is compared to both alternative homozygous forms, or the response of heterozygous patients is grouped with the response of one class of homozygous patients and said group is compared to the response of the alternative homozygous group.

Such methods can utilize either retrospective or prospective information concerning treatment response variability. Thus, in a preferred embodiment, it is previously known that patient response to the method of treatment is variable.

Also in preferred embodiments, the disease or condition is as for other aspects of this invention; for example, the treatment involves administration of a compound or pharmaceutical composition.

In preferred embodiments, the method involves a clinical trial, e.g., as described herein. Such a trial can be arranged, for example, in any of the ways described herein, e.g., in the Detailed Description.

The present invention also provides methods of treatment of a disease or condition as identified herein. Such methods combine identification of the presence or absence of particular variances, preferably in a gene or genes from Tables 1-6, 12-17, and 18-23, with the administration of a compound; identification of the presence of particular variances with selection of a method of treatment and

administration of the treatment; and identification of the presence or absence of particular variances with elimination of a method of treatment based on the variance information indicating that the treatment is likely to be ineffective or contra-indicated, and thus selecting and administering an alternative treatment effective
5 against the disease or condition. Thus, preferred embodiments of these methods incorporate preferred embodiments of such methods as described for such sub-aspects.

As used herein, a "gene" is a sequence of DNA present in a cell that directs the expression of a "biologically active" molecule or "gene product", most
10 commonly by transcription to produce RNA and translation to produce protein. The "gene product" is most commonly a RNA molecule or protein or a RNA or protein that is subsequently modified by reacting with, or combining with, other constituents of the cell. Such modifications may include, without limitation, modification of proteins to form glycoproteins, lipoproteins, and phosphoproteins, or other
15 modifications known in the art. RNA may be modified without limitation by polyadenylation, splicing, capping or export from the nucleus or by covalent or noncovalent interactions with proteins.. The term "gene product" refers to any product directly resulting from transcription of a gene. In particular this includes partial, precursor, and mature transcription products (i.e., pre-mRNA and mRNA),
20 and translation products with or without further processing including, without limitation, lipidation, phosphorylation, glycosylation, or combinations of such processing

The term "gene involved in the origin or pathogenesis of a disease or condition" refers to a gene that harbors mutations or polymorphisms that contribute
25 to the cause of disease, or variances that affect the progression of the disease or expression of specific characteristics of the disease. The term also applies to genes involved in the synthesis, accumulation, or elimination of products that are involved in the origin or pathogenesis of a disease or condition including, without limitation, proteins, lipids, carbohydrates, hormones, or small molecules.

The term "gene involved in the action of a drug" refers to any gene whose gene product affects the efficacy or safety of the drug or affects the disease process being treated by the drug, and includes, without limitation, genes that encode gene products that are targets for drug action, gene products that are involved in the metabolism, activation or degradation of the drug, gene products that are involved in
35 the bioavailability or elimination of the drug to the target, gene products that affect biological pathways that, in turn, affect the action of the drug such as the synthesis or degradation of competitive substrates or allosteric effectors or rate-limiting reaction, or, alternatively, gene products that affect the pathophysiology of the

disease process via pathways related or unrelated to those altered by the presence of the drug compound. (Particular variances in the latter category of genes may be associated with patient groups in whom disease etiology is more or less susceptible to amelioration by the drug. The "action" of a drug refers to its effect on biological products within the body. The action of a drug also refers to its effects on the signs or symptoms of a disease or condition, or effects of the drug that are unrelated to the disease or condition leading to unanticipated effects on other processes. Such unanticipated processes often lead to adverse events or toxic effects. The terms "adverse event" or "toxic" event" are known in the art and include, without limitation, those listed in the FDA reference system for adverse events.

In accordance with the aspects above and the Detailed Description below, there is also described for this invention an approach for developing drugs that are explicitly indicated for, and/or for which approved use is restricted to or recommended to be restricted to individuals in the population with specific variances or combinations of variances, as determined by diagnostic tests for variances or variant forms of certain genes involved in the disease or condition or involved in the action or metabolism or transport of the drug. Such drugs may provide more effective treatment for a disease or condition in a population identified or characterized with the use of a diagnostic test for a specific variance or variant form of the gene if the gene is involved in the action of the drug or in determining a characteristic of the disease or condition. Such drugs may be developed using the diagnostic tests for specific variances or variant forms of a gene to determine the inclusion of patients in a clinical trial.

Thus, the invention also provides a method for producing a pharmaceutical composition by identifying a compound which has differential activity or effectiveness against a disease or condition in patients having at least one variance in a gene, preferably in a gene from Tables 1-6, compounding the pharmaceutical composition by combining the compound with a pharmaceutically acceptable carrier, excipient, or diluent such that the composition is preferentially effective in patients who have at least one copy of the variance or variances. In some cases, the patient has two copies of the variance or variances. In preferred embodiments, the disease or condition, gene or genes, variances, methods of administration, or method of determining the presence or absence of variances is as described for other aspects of this invention. In preferred embodiments, the active component of the pharmaceutical composition is a compound listed in the compound tables below (Tables 24 through 68), or a compound chemically related to one of the listed compounds.

Similarly, the invention provides a method for producing a pharmaceutical agent by identifying a compound which has differential activity against a disease or condition in patients having at least one copy of a form of a gene, preferably a gene from Tables 1 through 6, having at least one variance and synthesizing the compound in an amount sufficient to provide a pharmaceutical effect in a patient suffering from the disease or condition. The compound can be identified by conventional screening methods and its activity confirmed. For example, compound libraries can be screened to identify compounds which differentially bind to products of variant forms of a particular gene product, or which differentially affect expression of variant forms of the particular gene, or which differentially affect the activity of a product expressed from such gene. Alternatively, the design of a compound can exploit knowledge of the variances provided herein to avoid significant allele specific effects, in order to reduce the likelihood of significant pharmacogenetic effects during the clinical development process. Preferred embodiments are as for the preceding aspect.

In another aspect, the invention provides a method of treating a disease or condition in a patient by selecting a patient whose cells have an allele of an identified gene, preferably a gene selected from the genes listed in Tables 1 through 6. The allele contains at least one variance correlated with more effective response to a treatment of said disease or condition. The method also includes altering the level of activity in cells of the patient of a product of the allele, where the altering provides a therapeutic effect.

Preferably the allele contains a variance as shown in Tables 1-6, 12-17, and 18-23, or other variance table herein, or in Table 1 or 3 of Stanton et al., U.S. Application No. 09/300,747. Also preferably, the altering involves administering to the patient a compound preferentially active on at least one but less than all alleles of the gene.

Preferred embodiments include those as described above for other aspects of treating a disease or condition.

As recognized by those skilled in the art, all the methods of treating described herein include administration of the treatment to a patient.

In a further aspect, the invention provides a method for determining a treatment effective to treat a disease or condition by altering the level of activity of a product of an allele of a gene selected from the genes listed in Tables 1-6, and determining whether that alteration provides a differential effect (with respect to reducing or alleviating a disease or condition, or with respect to variation in toxicity or tolerance to a treatment) in patients with at least one copy of at least one allele of the gene as compared to patients with at least one copy of one alternative allele.,

The presence of such a differential effect indicates that altering the level or activity of the gene provides at least part of an effective treatment for the disease or condition.

Preferably the method for determining a treatment is carried out in a clinical trial, e.g., as described above and/or in the Detailed Description below.

In a further aspect, the invention provides a method for determining a treatment effective to treat a disease or condition by altering the level of activity of a product of an allele of a gene selected from the genes listed in Tables 1-6, and determining whether that alteration provides a differential effect (with respect to reducing or alleviating a disease or condition, or with respect to variation in toxicity or tolerance to a treatment) in patients with at least one copy of at least one allele of the gene as compared to patients with at least one copy of one alternative allele. The presence of such a differential effect indicates that altering the level or activity of the gene provides at least part of an effective treatment for the disease or condition.

Preferably the method for determining a method of treatment is carried out in a clinical trial, e.g., as described above and/or in the Detailed Description below.

In still another aspect, the invention provides a method for performing a clinical trial or study, which includes selecting or stratifying subjects in the trial or study using a variance or variances or haplotypes from one or more genes specified in Tables 1-6, 12-17, and 18-23. Preferably the differential efficacy, tolerance, or safety of a treatment in a subset of patients who have a particular variance, variances, or haplotype in a gene or genes from Tables 1-6, 12-17, and 18-23 is determined by conducting a clinical trial and using a statistical test to assess whether a relationship exists between efficacy, tolerance, or safety and the presence or absence of any of the variances or haplotype in one or more of the genes. Results of the clinical trial or study are indicative of whether a higher or lower efficacy, tolerance, or safety of the treatment in a subset of patients is associated with any of the variance or variances or haplotype in one or more of the genes. In preferred embodiments, the clinical trial or study is a Phase I, II, III, or IV trial or study. Preferred embodiments include the stratifications and/or statistical analyses as described below in the Detailed Description.

In preferred embodiments, normal subjects or patients are prospectively stratified by genotype in different genotype-defined groups, including the use of genotype as an enrollment criterion, using a variance, variances or haplotypes from

Tables 1-6, 12-17, and 18-23, and subsequently a biological or clinical response variable is compared between the different genotype-defined groups. In preferred embodiments, normal subjects or patients in a clinical trial or study are stratified by a biological or clinical response variable in different biologically or clinically-defined groups, and subsequently the frequency of a variance, variances or haplotypes from Tables 1-6, 12-17, and 18-23 is measured in the different biologically or clinically defined groups.

In preferred embodiments, e.g., of the above two analyses, the normal subjects or patients in a clinical trial or study are stratified by at least one demographic characteristic selected from the groups consisting of sex, age, racial origin, ethnic origin, or geographic origin.

Generally the method will involve assigning patients to a group to receive the method of treatment or to a control group.

In yet another aspect, the invention provides experimental methods for finding additional variances in a gene provided in Tables 1-6, 12-17, 18-23. A number of experimental methods can also beneficially be used to identify variances. Thus, the invention provides methods for producing cDNA (Example 1) and detecting additional variances in the genes provided in Tables 1-6, 12-17, 18-23, using the single strand conformation polymorphism (SSCP) method (Example 2), the T4 Endonuclease VII method (Example 3) or DNA sequencing (Example 4) or other methods pointed out below. The application of these methods to the identified genes will provide identification of additional variances that can affect inter-individual variation in drug or other treatment response. One skilled in the art will recognize that many methods for experimental variance detection have been described (in addition to the exemplary methods of examples 2, 3, 4) and can be utilized. These additional methods include chemical cleavage of mismatches (see, e.g., Ellis T.P., et al., Chemical cleavage of mismatch: a new look at an established method. *Human Mutation* 11(5):345-53, 1998), denaturing gradient gel electrophoresis (see, e.g., Van Orsouw N.J., et al., Design and application of 2-D DGGE-based gene mutational scanning tests. *Genet Anal.* 14(5-6):205-13, 1999) and heteroduplex analysis (see, e.g., Ganguly A., et al., Conformation-sensitive gel electrophoresis for rapid detection of single-base differences in double-stranded PCR products and DNA fragments: evidence for solvent-induced bends in DNA heteroduplexes. *Proc Natl Acad Sci U S A.* 90 (21):10325-9, 1993). Table 3 of Stanton et al., U.S. Application No. 09/300,747, provides a description of the additional possible variances that could be detected by one skilled in the art by

testing an identified gene in Tables 1-6, 12-17, 18-23, using the variance detection methods described or other methods which are known or are developed.

The present invention provides a method for treating a patient at risk for a disease, disorder, dysfunction or condition (for example to prevent or delay the onset of frank disease) or a patient already diagnosed with a said disease or a disease associated with said disease. The methods include identifying such a patient and determining the patient's genotype or haplotype for an identified gene or genes. The patient identification can, for example, be based on clinical evaluation using conventional clinical metrics and/or on evaluation of a genetic variance or variances in one or more genes, preferably a gene or genes from Tables 1-6. The invention provides a method for using the patient's genotype status to determine a treatment protocol that includes a prediction of the efficacy and/or safety of a therapy.

In another aspect, the invention provides a method for treating a patient at risk for a drug-induced disease, disorder or dysfunction by a) identifying a patient with such a risk, b) determining the genotypic allele status of the patient, and c) converting the data obtained in step b) into a treatment protocol that includes a comparison of the genotypic allele status determination with the allele frequency of a control population. This comparison allows for a statistical calculation of the patient's risk for having drug-induced disease, disorder, or dysfunction, e.g., based on correlation of the allele frequencies for a population with response or disease occurrence and/or severity. In preferred embodiments, the method provides a treatment protocol that predicts a patient being heterozygous or homozygous for an identified allele to exhibit signs and or symptoms of drug-induced disease, disorder, or dysfunction and a patient who is wild-type homozygous for the said allele, as responding favorably to these therapies.

In another related aspect, the invention provides a method for identifying a patient for participation in a clinical trial of a therapy for the treatment of a disease or an associated pathological or psychiatric condition.

The method for identification of a subject of the participation in a clinical trial of a therapy for a disease described in this invention involves determining the genotype or haplotype of a patient with (or at risk for) a disease as identified herein. Preferably the genotype is for a variance in a gene from Tables 1-6. Patients with eligible genotypes are then assigned to a treatment or placebo group, preferably by a blinded randomization procedure. In preferred embodiments, the selected patients have at least no copies, one copy or two copies of a wild type specific allele of identified a gene or genes identified in Tables 1-6. Alternatively, patients selected for the clinical trial may have zero, one or two copies of an allele belonging to a set of alleles, where the set of alleles comprise a group of related alleles. One

procedure for rigorously defining a set of alleles is by applying phylogenetic methods to the analysis of haplotypes. (See, for example: Templeton A.R., Crandall K.A. and C.F. Sing, A cladistic analysis of phenotypic associations with haplotypes inferred from restriction endonuclease mapping and DNA sequence data. III.

5 Cladogram estimation. *Genetics* 1992 Oct. 132(2):619-33.) Regardless of the specific tools used to group alleles, the trial would then test the hypothesis that a statistically significant difference in response to a treatment can be demonstrated between two groups of patients each defined by the presence of zero, one or two alleles (or allele groups) at a gene or genes. Said response may be a desired or an
10 undesired response. In a preferred embodiment, the treatment protocol involves a comparison of placebo vs. treatment response rates in two or more genotype-defined groups. For example a group with no copies of an allele may be compared to a group with two copies, or a group with no copies may be compared to a group consisting of those with one or two copies. In this manner different genetic models (dominant, co-dominant, recessive) for the transmission of a treatment response trait
15 can be tested. Alternatively, statistical methods that do not posit a specific genetic model, such as contingency tables, can be used to measure the effects of an allele on treatment response.

In another preferred embodiment, patients in a clinical trial can be grouped
20 (at the end of the trial) according to treatment response, and statistical methods can be used to compare allele (or genotype or haplotype) frequencies in two groups. For example responders can be compared to nonresponders, or patients suffering adverse events can be compared to those not experiencing such effects. Alternatively response data can be treated as a continuous variable and the ability of genotype to
25 predict response can be measured. In a preferred embodiments patients who exhibit extreme phenotypes are compared with all other patients or with a group of patients who exhibit a divergent extreme phenotype. For example if there is a continuous or semi-continuous measure of treatment response (for example the Alzheimer's Disease Assessment Scale, the Mini-Mental State Examination or the Hamilton
30 Depression Rating Scale) then the 10% of patients with the most favorable responses could be compared to the 10% with the least favorable, or the patients one standard deviation above the mean score could be compared to the remainder, or to those one standard deviation below the mean score. One useful way to select the threshold for defining a response is to examine the distribution of responses in a placebo group. If
35 the upper end of the range of placebo responses is used as a lower threshold for an 'outlier response' then the outlier response group should be almost free of placebo responders. This is a useful threshold because the inclusion of placebo responders in

a 'true' reponse group decreases the ability of statistical methods to detect a genetic difference between responders and nonresponders.
disease.

In a related aspect, the invention provides a method for developing a disease management protocol that entails diagnosing a patient with a disease or a disease susceptibility, determining the genotype of the patient at a gene or genes correlated with treatment response and then selecting an optimal treatment based on the disease and the genotype (or genotypes or haplotypes). The disease management protocol may be useful in an education program for physicians, other caregivers or pharmacists; may constitute part of a drug label; or may be useful in a marketing campaign.

In a related aspect, the invention provides a method for treating a patient at risk for or diagnosed with drug-induced disease or pathological condition or dysfunction using the methods of the above aspect and conducting a step c) which involves determining the gene allele load status of the patient. This method further involves converting the data obtained in steps b) and c) into a treatment protocol that includes a comparison of the allele status determinations of these steps with the allele frequency of a control population. This affords a statistical calculation of the patient's risk for having drug-induced disease, disorder or dysfunction. In a preferred embodiment, the method is useful for identifying drug-induced disease, disorder or dysfunction. In addition, in related embodiments, the methods provide a treatment protocol that predicts a patient to be at high risk for drug-induced disease, disorder or dysfunction responding by exhibiting signs and symptoms of drug-induced toxicity, disorders, dysfunction if the patient is determined as having a genotype or allelic difference in the identified gene or genes. Such patients are preferably given alternative therapies.

The invention also provides a method for improving the safety of candidate therapies for the identification of a drug-induced disease, disorder, or dysfunction. The method includes the step of comparing the relative safety of the candidate therapeutic intervention in patients having different alleles in one or more than one of the genes listed in Tables 1-6, 12-17, and 18-23. Preferably, administration of the drug is preferentially provided to those patients with an allele type associated with increased efficacy. In a preferred embodiment, the alleles of identified gene or genes used are wild-type and those associated with altered biological activity.

For the aspects above, in connection with any of the listed diseases, disorders, or conditions and treatments thereof, or indeed any disease or disorder, can utilize pharmacogenetic information and determinations of genes and gene pathways involved in the absorption, distribution, metabolism, or excretion of said

treatment. Thus, the presence or the absence of at least variance or haplotype in such a gene or genes can be indicative of the effectiveness of a treatment for a given disease, disorder, or condition, where the gene or gene pathway is involved in the absorption, distribution, metabolism, or excretion of said treatment, e.g., a drug treatment.

As used herein, by “therapy associated with drug-induced disease” is meant any therapy resulting in pathophysiologic dysfunction or signs and symptoms of failure or dysfunction, or those associated with the pathophysiological manifestations of a disorder. A suitable therapy can be a pharmacological agent, drug, or therapy that alters a pathways identified to affect the molecular structure or function of the parent candidate therapeutic intervention thereby affecting drug-induced disease or disorder progression of any of the described organ system dysfunctions.

By “drug-induced disease” or “drug-induced syndrome” is meant any physiologic condition that may be correlated with medical therapy by a drug, agent, or candidate therapeutic intervention.

By “drug-induced dysfunction” is meant a physiologic disorder or syndrome that may be correlated with medical therapy by a drug, agent, or candidate therapeutic intervention in which symptomology is similar to drug-induced disease. Specifically included are: a) hemostasis dysfunction; b) cutaneous disorders; c) cardiovascular dysfunction; d) renal dysfunction; e) pulmonary dysfunction; f) hepatic dysfunction; g) systemic reactions; and h) central nervous system dysfunction.

By “drug associated disorder” is meant a physiologic dysfunction that may be correlated with medical therapy by a drug, agent, or candidate therapeutic intervention. The drug associated disorder may include disease, disorder, or dysfunction.

As used herein, by “therapy associated with inflammatory or immunological disease” is meant any therapy resulting in dysfunction or signs and symptoms of a inflammatory or immunologic condition or dysfunction, or those associated with the pathophysiological manifestations of a clinically diagnosed inflammatory or immunologic disorder or syndrome. A suitable therapy can be a pharmacological agent or drug that may enhance or inhibit metabolic pathways identified to affect the molecular structure or function of the parent candidate therapeutic intervention thereby affecting inflammatory or immunological disease progression of any of these inflammatory or immunological dysfunctions.

By “inflammatory or immunological dysfunction” is meant a disease or syndrome in which symptomology is similar to a inflammatory or immunological

disease. Specifically included are: arthritis, asthma, chronic obstructive pulmonary disease, autoimmune disease, inflammatory bowel disease, immunosuppression related to transplantation, pain associated with inflammation, psoriasis, atherosclerosis, and hepatitis.

5 By "pathway" or "gene pathway" is meant the group of biologically relevant genes involved in a pharmacodynamic or pharmacokinetic mechanism of drug, agent, or candidate therapeutic intervention. These mechanisms may further include any physiologic effect the drug or candidate therapeutic intervention renders.

10 By "disease management protocol" or "treatment protocol" is meant a means for devising a therapeutic plan for a patient using laboratory, clinical and genetic data, including the patient's diagnosis and genotype. The protocol clarifies therapeutic options and provides information about probable prognoses with different treatments. The treatment protocol may the provide an estimate of the likelihood that a patient will respond positively or negatively to a therapeutic
15 intervention. The treatment protocol may also provide guidance regarding optimal drug dose and administration, and likely timing of recovery or rehabilitation. A "disease management protocol" or "treatment protocol" may also be formulated for asymptomatic and healthy subjects in order to forecast future disease risks based on laboratory, clinical and genetic variables. In this setting the protocol specifies
20 optimal preventive or prophylactic interventions, including use of compounds, changes in diet or behavior, or other measures. The treatment protocol may include the use of a computer program.

In another aspect, the invention provides a kit containing at least one probe or at least one primer (or other amplification oligonucleotide) or both (e.g., as described
25 above) corresponding to a gene or genes listed in Tables 1-6, 12-17, and 18-23 or other gene related to a disease or condition listed in Tables 7-11 or described within the invention. The kit is preferably adapted and configured to be suitable for identification of the presence or absence of a particular variance or variances, which can include or consist of a nucleic acid sequence corresponding to a portion of a gene. A plurality of variances
30 may comprise a haplotype of haplotypes. The kit may also contain a plurality of either or both of such probes and/or primers, e.g., 2, 3, 4, 5, 6, or more of such probes and/or primers. Preferably the plurality of probes and/or primers are adapted to provide detection of a plurality of different sequence variances in a gene or plurality of genes, e.g., in 2, 3, 4, 5, or more genes or to amplify and/or sequence a nucleic acid sequence
35 including at least one variance site in a gene or genes. Preferably one or more of the variance or variances to be detected are correlated with variability in a treatment response or tolerance, and are preferably indicative of an effective response to a treatment. In preferred embodiments, the kit contains components (e.g., probes and/or primers) adapted

or useful for detection of a plurality of variances (which may be in one or more genes) indicative of the effectiveness of at least one treatment, preferably of a plurality of different treatments for a particular disease or condition. It may also be desirable to provide a kit containing components adapted or useful to allow detection of a plurality of variances indicative of the effectiveness of a treatment or treatment against a plurality of diseases. The kit may also optionally contain other components, preferably other components adapted for identifying the presence of a particular variance or variances. Such additional components can, for example, independently include a buffer or buffers, e.g., amplification buffers and hybridization buffers, which may be in liquid or dry form, a DNA polymerase, e.g., a polymerase suitable for carrying out PCR (e.g., a thermostable DNA polymerase), and deoxy nucleotide triphosphates (dNTPs). Preferably a probe includes a detectable label, e.g., a fluorescent label, enzyme label, light scattering label, or other label. Preferably the kit includes a nucleic acid or polypeptide array on a solid phase substrate. The array may, for example, include a plurality of different antibodies, and/or a plurality of different nucleic acid sequences. Sites in the array can allow capture and/or detection of nucleic acid sequences or gene products corresponding to different variances in one or more different genes. Preferably the array is arranged to provide variance detection for a plurality of variances in one or more genes which correlate with the effectiveness of one or more treatments of one or more diseases, which is preferably a variance as described herein.

The kit may also optionally contain instructions for use, which can include a listing of the variances correlating with a particular treatment or treatments for a disease or diseases and/or a statement or listing of the diseases for which a particular variance or variances correlates with a treatment efficacy and/or safety.

Preferably the kit components are selected to allow detection of a variance described herein, and/or detection of a variance indicative of a treatment, e.g., administration of a drug, pointed out herein.

Additional configurations for kits of this invention will be apparent to those skilled in the art.

The invention also includes the use of such a kit to determine the genotype(s) of one or more individuals with respect to one or more variance sites in one or more genes identified herein. Such use can include providing a result or report indicating the presence and/or absence of one or more variant forms or a gene or genes which are indicative of the effectiveness of a treatment or treatments.

In another aspect, the invention provides a method for determining whether there is a genetic component to intersubject variation in a surrogate treatment response. The method involves administering the treatment to a group of related (preferably normal) subjects and a group of unrelated (preferably normal) subjects, measuring a surrogate pharmacodynamic or pharmacokinetic drug response variable in the subjects, performing a statistical test measuring the variation in response in the group of related subjects and, separately in the group of unrelated subjects, comparing the magnitude or pattern of variation in response or both between the groups to determine if the responses of the groups are different, using a predetermined statistical measure of difference. A difference in response between the groups is indicative that there is a genetic component to intersubject variation in the surrogate treatment response.

In preferred embodiments, the size of the related and unrelated groups is set in order to achieve a predetermined degree of statistical power.

In another aspect, the invention provides a method for evaluating the combined contribution of two or more variances to a surrogate drug response phenotype in subjects (preferably normal subjects) by a. genotyping a set of unrelated subjects participating in a Phase I trial of a compound. The genotyping is for two or more variances (which can be a haplotype), thereby identifying subjects with specific genotypes, where the two or more specific genotypes define two or more genotype-defined groups. A drug is administered to subjects with two or more of the specific genotypes, and a surrogate pharmacodynamic or pharmacokinetic drug response variable is measured in the subjects. A statistical test or tests is performed to measure response in the groups separately, where the statistical tests provide a measurement of variation in response with each group. The magnitude or pattern of variation in response or both is compared between the groups to determine if the groups are different using a predetermined statistical measure of difference.

In preferred embodiments, the specific genotypes are homozygous genotypes for two variances. In preferred embodiments, the comparison is between groups of subjects differing in three or more variances, e.g., 3, 4, 5, 6, or even more variances.

In another aspect, the invention provides a method for providing contract research services to clients (preferably in the pharmaceutical and biotechnology industries), by enrolling subjects (e.g., normal and/or patient subjects) in a clinical

drug trial or study unit (preferably a Phase I drug trial or study unit) for the purpose of genotyping the subjects in order to assess the contribution of genetic variation to variation in drug response, genotyping the subjects to determine the status of one or more variances in the subjects, administering a compound to the subjects and
5 measuring a surrogate drug response variable, comparing responses between two or more genotype-defined groups of subjects to determine whether there is a genetic component to the interperson variability in response to said compound; and reporting the results of the Phase I drug trial to a contracting entity. Clearly, intermediate results, e.g., response data and/or statistical analysis of response or
10 variation in response.

In preferred embodiments, at least some of the subjects have disclosed that they are related to each other and the genetic analysis includes comparison of groups of related individuals. To encourage participation of sufficient numbers of related individuals, it can be advantageous to offer or provide compensation to one or more
15 of the related individuals based on the number of subjects related to them who participate in the clinical trial, or on whether at least a minimum number of related subjects participate, e.g., at least 3, 5, 10, 20, or more.

In a related aspect, the invention provides a method for recruiting a clinical trial population for studies of the influence of genetic variation on drug response, by
20 soliciting subjects to participate in the clinical trial, obtaining consent of each of a set of subjects for participation in the clinical trial, obtaining additional related subjects for participation in the clinical trial by compensating one or more of the related subjects for participation of their related subjects at a level based on the number of related subjects participating or based on participation of at least a
25 minimum specified number of related subjects, e.g., at minimum levels as specified in the preceding aspect.

In all of the aspects herein, the gene (or genes) can be a gene as identified herein (e.g., in the Detailed Description, including examples, or Tables 1-6, 12-17, or 18-23, or is in a pathway as identified herein, e.g., in a Table.

30 By "pathway" or "gene pathway" is meant the group of biologically relevant genes involved in a pharmacodynamic or pharmacokinetic mechanism of drug, agent, or candidate therapeutic intervention. These mechanisms may further include any physiologic effect the drug or candidate therapeutic intervention renders.

Included in this are "biochemical pathways" which is used in its usual sense to refer to a series of related biochemical processes (and the corresponding genes and gene products) involved in carrying out a reaction or series of reactions. Generally in a cell, a pathway performs a significant process in the cell.

5 By "pharmacological activity" used herein is meant a biochemical or physiological effect of drugs, compounds, agents, or candidate therapeutic interventions upon administration and the mechanism of action of that effect.

The pharmacological activity is then determined by interactions of drugs, compounds, agents, or candidate therapeutic interventions, or their mechanism of action, on their target proteins or macromolecular components. By "agonist" or
10 "mimetic" or "activators" is meant a drug, agent, or compound that activate physiologic components and mimic the effects of endogenous regulatory compounds. By "antagonists", "blockers" or "inhibitors" is meant drugs, agents, or compounds that bind to physiologic components and do not mimic endogenous
15 regulatory compounds, or interfere with the action of endogenous regulatory compounds at physiologic components. These inhibitory compounds do not have intrinsic regulatory activity, but prevent the action of agonists. By "partial agonist" or "partial antagonist" is meant an agonist or antagonist, respectively, with limited or partial activity. By "negative agonist" or "inverse antagonists" is meant that a
20 drug, compound, or agent that can interact with a physiologic target protein or macromolecular component and stabilizes the protein or component such that agonist-dependent conformational changes of the component do not occur and agonist mediated mechanism of physiological action is prevented. By "modulators" or "factors" is meant a drug, agent, or compound that interacts with a target protein
25 or macromolecular component and modifies the physiological effect of an agonist.

As used herein the term "chemical class" refers to a group of compounds that share a common chemical scaffold but which differ in respect to the substituent groups linked to the scaffold. Examples of chemical classes of drugs include, for example, phenothiazines, piperidines, benzodiazepines and aminoglycosides.

30 Members of the phenothiazine class include, for example, compounds such as chlorpromazine hydrochloride, mesoridazine besylate, thioridazine hydrochloride, acetophenazine maleate trifluoperazine hydrochloride and others, all of which share a phenothiazine backbone. Members of the piperidine class include, for example,

compounds such as meperidine, diphenoxylate and loperamide, as well as phenylpiperidines such as fentanyl, sufentanil and alfentanil, all of which share the piperidine backbone. Chemical classes and their members are recognized by those skilled in the art of medicinal chemistry.

5 As used herein the term "surrogate marker" refers to a biological or clinical parameter that is measured in place of the biologically definitive or clinically most meaningful parameter. In comparison to definitive markers, surrogate markers are generally either more convenient, less expensive, provide earlier information or provide pharmacological or physiological information not directly obtainable with
10 definitive markers. Examples of surrogate biological parameters: (i) testing erythrocyte membrane acetylcholinesterase levels in subjects treated with an acetylcholinesterase inhibitor intended for use in Alzheimer's disease patients (where inhibition of brain acetylcholinesterase would be the definitive biological parameter); (ii) measuring levels of CD4 positive lymphocytes as a surrogate marker
15 for response to a treatment for acquired immune deficiency syndrome (AIDS). Examples of surrogate clinical parameters: (i) performing a psychometric test on normal subjects treated for a short period of time with a candidate Alzheimer's compound in order to determine if there is a measurable effect on cognitive function. The definitive clinical test would entail measuring cognitive function in a clinical
20 trial in Alzheimer's disease patients. (ii) Measuring blood pressure as a surrogate marker for myocardial infarction. The measurement of a surrogate marker or parameter may be an endpoint in a clinical study or clinical trial, hence "surrogate endpoint".

As used herein the term "related" when used with respect to human subjects
25 indicates that the subjects are known to share a common line of descent; that is, the subjects have a known ancestor in common. Examples of preferred related subjects include sibs (brothers and sisters), parents, grandparents, children, grandchildren, aunts, uncles, cousins, second cousins and third cousins. Subjects less closely related than third cousins are not sufficiently related to be useful as "related"
30 subjects for the methods of this invention, even if they share a known ancestor, unless some related individuals that lie between the distantly related subjects are also included. Thus, for a group of related individuals, each subject shares a known ancestor within three generations or less with at least one other subject in the group,

and preferably with all other subjects in the group or has at least that degree of consanguinity due to multiple known common ancestors. More preferably, subjects share a common ancestor within two generations or less, or otherwise have equivalent level of consanguinity. Conversely, as used herein the term "unrelated", when used in respect to human subjects, refers to subjects who do not share a known ancestor within 3 generations or less, or otherwise have known relatedness at that degree.

As used herein the term "pedigree" refers to a group of related individuals, usually comprising at least two generations, such as parents and their children, but often comprising three generations (that is, including grandparents or grandchildren as well). The relation between all the subjects in the pedigree is known and can be represented in a genealogical chart.

As used herein the term "hybridization", when used with respect to DNA fragments or polynucleotides encompasses methods including both natural polynucleotides, non-natural polynucleotides or a combination of both. Natural polynucleotides are those that are polymers of the four natural deoxynucleotides (deoxyadenosine triphosphate [dA], deoxycytosine triphosphate [dC], deoxyguanine triphosphate [dG] or deoxythymidine triphosphate [dT], usually designated simply thymidine triphosphate [T]) or polymers of the four natural ribonucleotides (adenosine triphosphate [A], cytosine triphosphate [C], guanine triphosphate [G] or uridine triphosphate [U]). Non-natural polynucleotides are made up in part or entirely of nucleotides that are not natural nucleotides; that is, they have one or more modifications. Also included among non-natural polynucleotides are molecules related to nucleic acids, such as peptide nucleic acid [PNA]). Non-natural polynucleotides may be polymers of non-natural nucleotides, polymers of natural and non-natural nucleotides (in which there is at least one non-natural nucleotide), or otherwise modified polynucleotides. Non-natural polynucleotides may be useful because their hybridization properties differ from those of natural polynucleotides. As used herein the term "complementary", when used in respect to DNA fragments, refers to the base pairing rules established by Watson and Crick: A pairs with T or U; G pairs with C. Complementary DNA fragments have sequences that, when aligned in antiparallel orientation, conform to the Watson-Crick base pairing rules at all positions or at all positions except one. As used herein, complementary DNA

fragments may be natural polynucleotides, non-natural polynucleotides, or a mixture of natural and non-natural polynucleotides.

As used herein "amplify" when used with respect to DNA refers to a family of methods for increasing the number of copies of a starting DNA fragment.

5 Amplification of DNA is often performed to simplify subsequent determination of DNA sequence, including genotyping or haplotyping. Amplification methods include the polymerase chain reaction (PCR), the ligase chain reaction (LCR) and methods using Q beta replicase, as well as transcription-based amplification systems such as the isothermal amplification procedure known as self-sustained sequence
10 replication (3SR, developed by T.R. Gingeras and colleagues), strand displacement amplification (SDA, developed by G.T. Walker and colleagues) and the rolling circle amplification method (developed by P. Lizardi and D. Ward).

As used herein "contract research services for a client" refers to a business arrangement wherein a client entity pays for services consisting in part or in whole
15 of work performed using the methods described herein. The client entity may include a commercial or non-profit organization whose primary business is in the pharmaceutical, biotechnology, diagnostics, medical device or contract research organization (CRO) sector, or any combination of those sectors. Services provided to such a client may include any of the methods described herein, particularly
20 including clinical trial services, and especially the services described in the Detailed Description relating to a Pharmacogenetic Phase I Unit. Such services are intended to allow the earliest possible assessment of the contribution of a variance or variances or haplotypes, from one or more genes, to variation in a surrogate marker in humans. The surrogate marker is generally selected to provide information on a
25 biological or clinical response, as defined above.

As used herein, "comparing the magnitude or pattern of variation in response" between two or more groups refers to the use of a statistical procedure or procedures to measure the difference between two different distributions. For example, consider two genotype-defined groups, AA and aa, each homozygous for a
30 different variance or haplotype in a gene believed likely to affect response to a drug. The subjects in each group are subjected to treatment with the drug and a treatment response is measured in each subject (for example a surrogate treatment response). One can then construct two distributions: the distribution of responses in the AA

group and the distribution of responses in the aa group. These distributions may be compared in many ways, and the significance of any difference qualified as to its significance (often expressed as a p value), using methods known to those skilled in the art. For example, one can compare the means, medians or modes of the two
5 distributions, or one can compare the variance or standard deviations of the two distributions. Or, if the form of the distributions is not known, one can use nonparametric statistical tests to test whether the distributions are different, and whether the difference is significant at a specified level (for example, the $p < 0.05$ level, meaning that, by chance, the distributions would differ to the degree measured
10 less than one in 20 similar experiments). The types of comparisons described are similar to the analysis of heritability in quantitative genetics, and would draw on standard methods from quantitative genetics to measure heritability by comparing data from related subjects.

Another type of comparison that can be usefully made is between related and
15 unrelated groups of subjects. That is, the comparison of two or more distributions is of particular interest when one distribution is drawn from a population of related subjects and the other distribution is drawn from a group of unrelated subjects, both subjected to the same treatment. (The related subjects may consist of small groups of related subjects, each compared only to their relatives.) A comparison of the
20 distribution of a drug response variable (e.g. a surrogate marker) between two such groups may provide information on whether the drug response variable is under genetic control. For example, a narrow distribution in the group(s) of related subjects (compared to the unrelated subjects) would tend to indicate that the measured variable is under genetic control (i.e. the related subjects, on account of
25 their genetic homogeneity, are more similar than the unrelated individuals). The degree to which the distribution was narrower in the related individuals (compared to the unrelated individuals) would be proportionate to the degree of genetic control. The narrowness of the distribution could be quantified by, for example, computing variance or standard deviation. In other cases the shape of the distribution may not
30 be known and nonparametric tests may be preferable. Nonparametric tests include methods for comparing medians such as the sign test, the slippage test, or the rank correlation coefficient (the nonparametric equivalent of the ordinary correlation

coefficient). Pearson's Chi square test for comparing an observed set of frequencies with an expected set of frequencies can also be useful.

In addition to and in connection with the determination and utilization of pharmacogenetic information for treatment of proliferative disorders such as cancer, information provided by and genes identified in the following patents and applications are useful: Housman, INHIBITORS OF ALTERNATIVE ALLELES OF GENES ENCODING PROTEINS VITAL FOR CELL VIABILITY OR CELL GROWTH AS A BASIS FOR CANCER THERAPEUTIC AGENTS, U.S. Patent 5,702,890, issued December 30, 1997, and Housman et al., PCT/US98/05419, entitled TARGET GENES FOR ALLELE-SPECIFIC DRUGS. Essential and conditionally essential genes identified therein can be utilized as targets for the methods and compositions described in those documents. As an example of the use of the information provided by the listed references, LOH affecting a particular target gene provides information on the effect of a particular variance or variances in that target gene. This can be extended to evaluation of the effects of combinations of variations one or more genes subject to LOH. The utilization of conditionally essential genes is described further herein. For complete description, see the respective patent and application.

The inventors have also determined that the loss of chromosomes or chromosome segments that is characteristic of cancer cells (often termed loss of heterozygosity, or LOH) has an important interaction with gene sequence variances, in determining the effect of a treatment on a patient's cancer cells. Cancer cells with LOH may have only one copy of a gene that is present in two copies in normal cells. If the two normal copies (one inherited from each parent) differ in activity in a given patient, then the cancer cells will be functionally different from the normal cells on account of having only one of the two copies. For example, consider a patient heterozygous for high and low activity forms of a gene that metabolizes a cancer drug. If LOH involving the chromosome containing the gene has left cancer cells with only one copy of the gene then the metabolism of the drug will be different in cancer cells compared to normal cells. If the gene copy that is lost by LOH is the high activity version then cancer cells may experience higher levels of drug (due to slower metabolism) than normal cells. Provided in this invention are specific chromosomal sites characterized by LOH, and the frequency of LOH in different types of neoplasia at said sites. These LOH sites, in conjunction with the variances described above, may prove more useful in predicting response to treatment than variances alone. Methods for determining the combined impact of LOH and variances are described herein.

It was recognized that environmental factors can cause certain genes to be essential that are not essential under other conditions (including usual *in vivo* and culture conditions). For example, certain genes involved in intermediary metabolism are not essential if the cell or organism is supplemented with high concentrations of a particular nutrient or chemical entity, but if that nutrient or chemical entity is absent or present at low levels, the gene product is essential. In another example, the administration of a drug that inhibits one or more functions within the cell can cause other functions to be essential that are not essential in the absence of the drug. In another example, subjecting a cell to harsh physical agents, such as radiation, can cause certain genes to be essential that are not essential under normal conditions. Such genes are essential under certain conditions associated with the therapy of cancer. The demonstration that such genes are present in the population in more than one allelic form and are subjected to loss of heterozygosity in cancer or noncancer proliferative disorders makes such genes targets for allele specific drugs for the treatment of such disorders.

It was found that such genes, similar to generally essential genes, are frequently deleted due to LOH in cells of proliferative disorders such as cancers. Treatment methods involving such genes can provide enhanced sensitivity of cancer cells to a variety of different anti-proliferative treatments, including radiation and administration of various compounds. Unless otherwise indicated, the term "essential" includes both strictly essential and beneficial to cell growth or survival.

A gene is said to be "conditionally essential" if it is essential for cell survival or proliferation in a specific environmental condition differing from usual *in vivo* conditions or usual culture conditions for the type of cell, where the specific environmental condition is caused by the presence or absence of specific environmental constituents, pharmaceutical agents, including small molecules or biologicals, or physical factors such as radiation, or if the gene enhances the growth or survival of the cell under such conditions by at least 2-fold, preferably by at least 4-fold, and more preferably by at least 6-fold, 10-fold or even more.

Cancer cells, as well as cells from a number of different non-malignant proliferative disorders, from an individual almost invariably undergo a loss of genetic material (DNA) when compared to normal cells. Frequently, this deletion of genetic material includes the loss of one of the two alleles of genes for which the normal somatic cells of the same individual are heterozygous, meaning that there are differences in the sequence of the gene on each of the parental chromosomes. The loss of one allele in the cancer cells is referred to as "loss of heterozygosity" (LOH). Recognizing that almost all, if not all, varieties of cancer undergo LOH, and that regions of DNA loss are often quite extensive, the genetic content of deleted regions

in cancer cells was evaluated and it was found that a variety of different conditionally essential genes are frequently deleted, reducing the cancer cell to only one copy. In this context, the term "deleted" refers to the loss of one of two copies of a chromosome or sub-chromosomal segment. Further investigation demonstrated that the loss of genetic material from cancer cells sometimes results in the selective loss of one of two alleles of a particular gene at a particular locus or loci on a particular chromosome.

The term "proliferative disorder" refers to various cancers and disorders characterized by abnormal growth of somatic cells leading to an abnormal mass of tissue which exhibits abnormal proliferation, and consequently, the growth of which exceeds and is uncoordinated with that of the normal tissues. The abnormal mass of cells is referred to as a "tumor", where the term tumor can include both localized cell masses and dispersed cells. The term "cancer" refers to a neoplastic growth and is synonymous with the terms "malignancy", or "malignant tumor". The treatment of cancers and the identification of anticancer agents is the concern of particularly preferred embodiments of the aspects of the present invention. Other abnormal proliferative diseases include "nonmalignant tumors", and "dysplastic" conditions including, but not limited to, leiomyomas, endometriosis, benign prostate hypertrophy, atherosclerotic plaques, and dysplastic epithelium of lung, breast, cervix, or other tissues. Drugs used in treating cancer and other non-cancer proliferative disorders commonly aim to inhibit the proliferation of cells and are commonly referred to as antiproliferative agents.

"Loss of heterozygosity", "LOH", or "allele loss" refers to the loss of one of the alleles of a gene from a cell or cell lineage previously having two alleles of that gene. Normal cells contain two copies of each gene, one inherited from each parent. When these two genes differ in their gene sequence, the cell is said to be "heterozygous". The term heterozygous indicates that a cell contains two different allelic forms of a particular gene and thus indicates that the allelic forms differ at at least one sequence variance site. When one allele is lost in a cell, that cell and its progeny cells, comprising its cell lineage, become "hemizygous" for that gene or "partially hemizygous" for a set of genes, and heterozygosity is lost. LOH occurs in all cancers and is a common characteristic of non-malignant, proliferative disorders. In general, many different genes will be affected by loss of heterozygosity in a cell which undergoes loss of heterozygosity. In many cancers 10-40% of all of the genes in the human genome (there are estimated to be 60,000-100,000 different genes in the genome) will exhibit LOH. In the context of this invention, these terms refer preferably to loss of heterozygosity of a gene that has a particular sequence variance in normal somatic cells of an individual such that there is loss of heterozygosity with

respect to that particular sequence variance. Also preferably, these terms refer to loss of heterozygosity of a particular sequence variance that is recognized by an inhibitor that will inhibit one allele of the gene present in normal cells of the individual, but not an alternative allele.

5 The present invention provides a number of advantages. For example, the methods described herein allow for use of a determination of a patient's genotype for the timely administration of the most suitable therapy for that particular patient. The methods of this invention provide a basis for successfully developing and
10 obtaining regulatory approval for a compound even though efficacy or safety of the compound in an unstratified population is not adequate to justify approval. From the point of view of a pharmaceutical or biotechnology company, the information obtained in pharmacogenetic studies of the type described herein could be the basis of a marketing campaign for a drug. For example, a marketing campaign that
15 emphasized the superior efficacy or safety of a compound in a genotype or haplotype restricted patient population, compared to a similar or competing compound used in an undifferentiated population of all patients with the disease. In this respect a marketing campaign could promote the use of a compound in a genetically defined subpopulation, even though the compound was not intrinsically
20 superior to competing compounds when used in the undifferentiated population with the target disease. In fact even a compound with an inferior profile of action in the undifferentiated disease population could become superior when coupled with the appropriate pharmacogenetic test.

By "comprising" is meant including, but not limited to, whatever follows the
25 word "comprising". Thus, use of the term "comprising" indicates that the listed elements are required or mandatory, but that other elements are optional and may or may not be present. By "consisting of" is meant including, and limited to, whatever follows the phrase "consisting of". Thus, the phrase "consisting of" indicates that the listed elements are required or mandatory, and that no other elements may be
30 present. By "consisting essentially of" is meant including any elements listed after the phrase, and limited to other elements that do not interfere with or contribute to the activity or action specified in the disclosure for the listed elements. Thus, the phrase "consisting essentially of" indicates that the listed elements are required or mandatory, but that other elements are optional and may or may not be present
35 depending upon whether or not they affect the activity or action of the listed elements.

Other features and advantages of the invention will be apparent from the following description of the preferred embodiments thereof, and from the claims.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

First a brief description of the Tables is provided.

Tables 1-6. Gene Tables, lists genes that may be involved in
5 pharmacological response to cancer or other neoplastic disorders, neurological and
psychiatric, adsorption, distribution, metabolism, or excretion of, inflammation and
immune, endocrine and metabolism, and cardiovascular and renal therapeutics,
respectively, or that may define disease subsets with different prognosis and
consequent implications for treatment. These tables have seven columns. Column
10 1, headed "Class" provides broad groupings of genes relevant to the pharmacology
of indication-specific drugs. Column 2, headed "Pathway", provides a more detailed
categorization of the different classes of genes by indicating the overall purpose of
large groups of genes. These pathways contain genes implicated in the etiology or
treatment response of the various diseases detailed in Tables 7-11. Column 3,
15 headed "Function", further categorizes the pathways listed in column 2. Some
categories in column 2 (e.g. "Clotting") are not further categorized in column 3.

In column 4, headed "Name", lists the genes belonging to the class, pathway
and function shown to the left (in columns 1 – 3). The gene names given are
generally those used in the OMIM database or in GenBank, however one skilled in
20 the art will recognize that many genes have more than one name, and that it is a
straightforward task to identify synonymous names. For example, many alternate
gene names are provided in the OMIM record for a gene.

In column 5, headed "OMIM", the Online Mendelian Inheritance in Man
(OMIM) record number is listed for each gene in column 4. This record number
25 can be entered next to the words: "Enter one or more search keywords:" at the
OMIM world wide web site. The url is:
<http://www3.ncbi.nlm.nih.gov/Omim/searchomim.html>. An OMIM record exists for
most characterized human genes. The record often has useful information on the
chromosome location, function, alleles, and human diseases or disorders associated
30 with each gene.

In column 6, headed "GID", provides the GenBank identification number
(hence GID) of a genomic, cDNA, or partial sequence of the gene named in column
4. Usually the GID provides the record of a cDNA sequence. Many genes have
multiple Genbank accession numbers, representing different versions of a sequence
35 obtained by different research groups, or corrected or updated versions of a
sequence. As with the gene name, one skilled in the art will recognize that
alternative GenBank records related to the named record can be obtained easily. All
other GenBank records listing sequences that are alternate versions of the sequences

named in the table are equally suitable for the inventions described in this application. (One straightforward way to obtain additional GenBank records for a gene is on the internet. General instructions can be found at the NCBI web site at: <http://www3.ncbi.nlm.nih.gov>. More specifically, the GenBank record number in column 6 can be entered at the url:

<http://www3.ncbi.nlm.nih.gov/Entrez/nucleotide.html>. Once the GenBank record has been retrieved one can click on the "nucleotide neighbors" link and additional GenBank records from the same gene will be listed.action,

Column 7, headed "locus", provides the chromosome location of the gene listed on the same row. The chromosome location helps confirm the identity of the named gene if there is any ambiguity.

Tables 7-11 are matrix tables showing the intersection of genes and therapeutic indications – that is, which categories of genes are most likely to account for interpatient variation in response to treatments for which diseases. The first two columns provide a framework for organizing the genes listed in Tables 1-6. Column 1 is similar to the 'Class' column in Tables 1-6, while column 2 is a combination of the 'Pathway' and 'Function' columns in Tables 1-6. It is intended that the summary terms listed in columns 1 and 2 be read as referring to all the genes in the corresponding sections of Tables 1-6. The remaining columns in Tables 7-11 list the specific indications for a given disease category, for example in Table 7 there are thirteen neurological and psychiatric indications. The information in the Tables lies in the shaded boxes at the intersection of various 'Pathways' (the rows) and treatment indications. An intersection box is shaded when a row corresponding to a particular pathway (and by extension all the genes listed in that pathway in Tables 1-6) intersects a column for a specific neurological or psychiatric disease such that the pathway and genes are of possible use in explaining interpatient differences in response to treatments for the neurological or psychiatric indication.. Thus, the Tables enables one skilled in the art to identify therapeutically relevant genes in patients with one of the listed indications for the purposes of stratification of these patients based upon genotype and subsequent correlation of genotype with drug response. The shaded intersections indicate preferred sets of genes for understanding the basis of interpatient variation in response to therapy of the indicated disease indication, and in that respect are exemplary. Any of the genes in the tables may account for interpatient variation in response to treatments for any of the diseases listed. Thus, the shaded boxes indicate the gene pathways that one skilled in the art would first investigate in trying to understand interpatient variation in response to therapy for the listed neurological indications.

Tables 12-17 lists the exemplary DNA sequence variances in genes for therelevant to the methods described in the present invention. These variances were discovered by the inventors in studies of selected genes listed in Tables 1-6, and are provided here as useful for the methods of the present invention. The variances in

5 Tables 12-17 were discovered by one or more of the methods described below in the Detailed Description or Examples. The tables have eight columns. The column headings are spread over two rows, with five headings in the first row and three in the second row. The gene sequence variance listings in the tables have a similar organization to the column headings, with a set of nomenclature data in the first row

10 for each gene entry, and variance data in the second and additional following rows for however many sequence variances are available for a specific gene. Column 1, the "Name" column, contains the Human Genome Organization (HUGO) identifier for the gene. Column 2, the "GID" column provides the GenBank accession number of a genomic, cDNA, or partial sequence of a particular gene. Column 3, the

15 "OMIM_ID" column contains the record number corresponding to the Online Mendelian Inheritance in Man database for the gene provided in columns 1 and 2. This record number can be entered at the world wide web site <http://www3.ncbi.nlm.nih.gov/Omim/searchomim.html> to search the OMIM record on the gene. Column 4, the VGX_Symbol column, provides an internal identifier

20 for the gene. Column 5, the "Description" column provides a descriptive name for the gene, when available. Columns 6, 7 and 8 are on the second row of columns. Column 6, the "Variance_Start" column provides the nucleotide location of a variance with respect to the first listed nucleotide in the GenBank accession number provided in column 2. That is, the first nucleotide of the GenBank accession is

25 counted as nucleotide 1 and the variant nucleotide is numbered accordingly. Column 7, the "variance" column provides the nucleotide location of a variance with respect to an ATG codon believed to be the authentic ATG start codon of the gene, where the A of ATG is numbered as one (1) and the immediately preceding nucleotide is numbered as minus one (-1). This reading frame is important because

30 it allows the potential consequence of the variant nucleotide to be interpreted in the context of the gene anatomy (5' untranslated region, protein coding sequence, 3' untranslated region). Column 7 also provides the identity of the two variant nucleotides at the indicated position. Column 8, the "CDS_Context" column indicates whether the variance is in a coding region but silent (S); in a coding region

35 and results in an amino acid change (e.g., R347C, where the letters are one letter amino acid abbreviations and the number is the amino acid residue in the encoded amino acid sequence which is changed); in a sequence 5' to the coding region (5); or in a sequence 3' to the coding region (3). As indicated above, interpreting the

location of the variance in the gene is contingent on the correct assignment of the initial ATG of the encoded protein (the translation start site). It should be recognized that assignment of the correct ATG may occasionally be incorrect in GenBank, but that one skilled in the art will know how to carry out experiments to definitively identify the correct translation initiation codon (which is not always an ATG). In the event of any potential question concerning the proper identification of a gene or part of a gene, due for example, to an error in recording an identifier or the absence of one or more of the identifiers, the priority for use to resolve the ambiguity is GenBank accession number, OMIM identification number, HUGO identifier, common name identifier.

Tables 18-23 lists additional DNA sequence variances (in addition to those in Tables 12-17) in genes relevant to the methods of the present invention (i.e. selected genes from Tables 1-6). These variances were identified by various research groups and published in the scientific literature. The inventors realized that these variances may be useful for understanding interpatient variation in response to treatment of the diseases listed in Tables 7-11, and more generally useful for the methods of the present invention. The layout of Tables 18-23 is identical to that of Tables 12-17, and therefore the descriptions of the rows and columns in Tables 12-17 (above) pertain to Tables 18-23, as do the caveats and other remarks.

Tables 24-68 provide lists of exemplary compounds in clinical development for the various disease indications listed in Tables 7-11. The compounds listed in the tables are exemplary; that is, the methods of the invention will apply to other compounds as well. Each table has four columns. The first column is titled "Product Name", the second column is titled "Chemical Name", the third "Action" and the fourth "Indication". Under these headings are listed rows of compounds. For each compound there is a brief summary of information about the product name, its pharmacological action and potential clinical uses. The first column, "Product Name", provides the generic name and/or alphanumeric designation of the compound, as well as its trade name in some cases (in capital letters). The second column, "Chemical Name" provides the full chemical name of the compound. The listed compounds, or compounds chemically related to those listed (e.g. by modification of one or more chemical moieties of the listed compounds), are suitable for the methods of this invention. The third column, "Action", summarizes in a word or phrase an important pharmacological action of the compound, or what is currently believed to be an important pharmacological action – in most cases additional pharmacological actions are known but not listed to conserve space; alternatively, subsequent studies may reveal additional or alternative

pharmacological actions. (Sources listed in the detailed description will help clarify whether additional pharmacological actions have been discovered.) The fourth column, "Indication", provides an exemplary disease or condition for which the compound is currently being, or has already been, developed. In many cases the compound is being, has already been, or will likely be developed for other indications. Again, one skilled in the art will know how to identify additional drug development programs for these compounds. For example, a compound in development for one neurodegenerative disease is likely to be evaluated in the treatment of other neurodegenerative diseases.

Detailed Description

Preferred Embodiments

I. Disease Indications

A. Neurological and Psychiatric Diseases

5 The treatment of neurological and psychiatric diseases presents a challenge to physicians and other medical practitioners because the available therapeutics are only partially effective in only a fraction of patients. Further, many currently used medicines produce serious adverse effects. Therapeutic benefits and toxic side effects have to be balanced in each patient. This requires much attention to drug
10 selection, dosage adjustment and monitoring for potential adverse events on the part of care givers – effectively a new pharmacokinetic and pharmacodynamic study must be performed for each patient. These limitations of therapy are especially true of the most debilitating neurological and psychiatric diseases such as psychosis, depression, epilepticepilepsy, the neurodegenerative diseases including Alzheimer's
15 disease and Parkinson's disease, migraine and cerebrovascular disease. Although these diseases have distinct clinical presentations, havethere is extensive overlap in pathogenetic mechanisms and symptoms.

 Difficulties in treating neurological and psychiatric diseases are attributable to factors such as limited understanding of disease condition pathophysiology, lack
20 of specificity of pathophysiologic changes (i.e. variation in pathophysiologic machanisms in patients with similar clinical presentation) and lack of specificity of therapeutic compounds. Further, most medical therapy is directed to the amelioration of symptoms, not the arrest or reversal of underlying pathophysiologic processes. One good example of the difficulty of developing and marketing
25 effective treatments is the history of therapeutic candidates for Alzheimer's disease. Out of dozens of candidate treatments tested in clinical trials only two products have been approved for use in the United Statese, and one of them (tacrine; Cognex) has been withdrawn from marketing due to safety problems. Further, the one marketed product (donezepil; Aricept) is only used by a small fraction of eligible patients
30 because it has a reputation among caregivers and Alzheimer's disease advocacy groups as being ineffective in most patients. Thus a drug that enjoys a monopoly position in a major disease is not a great commercial success because its shortcomings are widely realized.

 In summary, medical management of neurological and psychiatric diseases is
35 empirical in nature, is only partially effective, and is associated with multiple undesirable side effects. In view of these clinical realities, the use of genetic tests to identify treatment responders, nonresponders, and/or those likely to develop undesirable side effects will have a major impact on use of existing classes of CNS

drugs, as well as on the development and use of new drugs to treat diseases of the central nervous system.

B. Pharmacokinetic Parameters and Effects on Efficacy

The pharmacokinetic parameters with potential effects on efficacy are absorption, distribution, metabolism, and excretion. These parameters affect efficacy broadly by modulating the availability of a compound at the site(s) of action. Interpatient variation in the availability of a compound drug, agent, or candidate therapeutic intervention can result in a reduction of the available compound or more compound at the site of action with a corresponding altered clinical effect. Differences in these parameters, therefore, can be a potential foundation of interpatient variability to drug response.

1. Pharmacokinetic Parameters that Result in a Reduction of Available Drug

- a. Absorption- Depending on the solubility of the drug, and its ability to passively cross membranes is fundamental to the ability of the drug, agent, or candidate therapeutic intervention to effectively enter the circulation and gain access to the principle site of action. For enteral delivery or administration, absorption is a critical first step in the pharmacologic process. Within the gastrointestinal tract, absorption of a drug, agent, or candidate therapeutic intervention can be affected by the pH of the contents, speed of gastric emptying, and presence of chelating or binding molecules to the drug, agent or candidate therapeutic intervention. Each of these parameters can effectively reduce the rate of passive absorption of the drug across the gastrointestinal mucosal membrane.
- b. Distribution- Once absorbed, the drug, agent or candidate therapeutic intervention must be delivered or distributed to the primary site of pharmacologic action. Although distribution is dependent on regional blood flow and cardiac output; distribution may be further affected by the rate and extent of sequestration of the drug into biological spaces that render the product unavailable to the principle or primary site of pharmacologic site of action. For example, many drugs are actively transported into biological compartments. These processes, if over- or under active may affect the availability and hence reduce the efficacy of the product. Further, only unbound drug may be effective to a cell, tissue, or physiological process, and bound product may be transported to a space that is physiologically unrelated to the pharmacologic mechanism of action or may be of deleterious adverse or toxic consequence.

- c. Metabolism- Induction of metabolic enzymes to covalently modify the parent drug, agent or candidate therapeutic intervention may reduce the ability of the parent drug to elicit a pharmacologic action. Metabolism may affect the target active site binding, rate and extent of distribution and excretion, and overall availability of the active molecule.
- d. Excretion- If the excretion of the drug or drug metabolite is rapid, less drug is available to elicit a pharmacologic effect.

2. Pharmacokinetic Parameters that Result in More Available Drug.

- a. Absorption- Enhanced absorption of drugs, agents or candidate therapeutic interventions may result in increased drug availability. For example, in some cases of decreased gastric emptying, there is an enhanced degree of absorption by prolonging contact with gastrointestinal mucosal membranes. In others, a change in the solubility of the drug may enhance the passive transport across the gastrointestinal mucosal membrane.
- b. Distribution- Since free drug is the form that renders pharmacologic action and is metabolised and excreted, drug binding may serve to protect the drug from mechanisms of inactivation. The rate and extent of drug binding affects the free drug concentration relative to the total concentration.
- c. Metabolism- If drug metabolism induction is occurring and the inducer is rapidly removed without adjustment in the dose of the drug, drug metabolism may be decreased and adverse effects or toxicities may occur.
- d. Excretion- If inhibition of active transport of the parent drug or metabolite across the bile cannicula or the renal tubule, there is a net result of enhanced drug availability.

C. Impaired Drug Tolerability and Drug-Induced Disease, Disorder, Dysfunction or Toxicity

In response to chemical substances, drugs, or xenobiotics, drug-induced disease, disorder, dysfunction, or toxicity manifests as cellular damage or organ physiologic dysfunction, with one potentially leading to the other.

Adverse drug reactions can be categorized as 1) mechanism based reactions which are exaggerations of pharmacologic effects and 2) idiosyncratic, unpredictable effects unrelated to the primary pharmacologic action. Although some

side effects appear shortly after administration of a drug, some side effects appear long after drug administration or after cessation of the drug. Furthermore, these reactions can be categorized by reversible or irreversible manifestations of the drug-induced toxicity referring to whether the clinical symptomology subsides or persists upon withdrawal of the offending agent.

In the first category, excessive drug effects may result from alterations of pharmacokinetic parameters by either drug-drug interactions, pathophysiologic disease mediated alterations in the organs or processes involved in absorption, distribution, metabolism, or excretion, or genetic predisposition to heightened pharmacodynamic effect of the drug. The excessive or heightened response may be receptor or drug target or non-receptor or non-drug target mediated.

There are a large number of adverse events that are suspected and or known to occur as a result of administration of a drug, agent, or candidate therapeutic intervention. For example, many antineoplastic agents act by prevention of cell division in dividing cells or promoting cytotoxicity via disruption of DNA synthesis, transcription, and formation of mitotic spindles. These agents, unfortunately, do not distinguish between normal and cancerous cells, e.g. normally dividing cells and cancer cells are equally killed. Therefore, adverse events of antineoplastic agents include bone marrow suppression leading to anemia, leukopenia, and thrombocytopenia; immunosuppression rendering the patient susceptible and vulnerable to infectious agents; and initiation of mutagenesis and the formation of alternate forms of cancer, in many cases, acute myeloid leukemia.

In another example of predictable adverse events related to drug therapy is immunosuppression as a result of therapy to reduce or ablate immune response. This therapy includes but is not exclusive to prevention of graft vs. host or autoimmune disease. These agents, e.g. corticosteroids, cyclosporine, and azathioprine, all suppress humoral or cell-mediated immunity. Patients taking these agents are rendered susceptible to microbial infections, particular opportunistic infections such as cytomegalovirus, pneumocystis carinii, Candida, and sperigillus. Furthermore, long-term immunosuppressive therapy is associated with increased risk of developing lymphoma. Individual drugs are associated with renal injury (cyclosporine) and interstitial pneumonitis (azathioprine).

In the second category of adverse events, idiosyncratic reactions arise often by unpredictable, unknown mechanisms or reactions that evoke immunologic reactions or unanticipated cytotoxicity.

Adverse reactions in this category are often found together, because often it is difficult to ascertain the etiology of the offending reaction. These toxic events can be specific for a target organ, e.g. ototoxicity, nephrotoxicity, hepatotoxicity,

neurotoxicity, etc. or are caused by reactive metabolic intermediates and are toxic or create local damage usually near the site of metabolism.

Immunologic reactions to drugs are thought or result from the combination of the drug or agent with a protein to form an antigenic protein-drug complex that stimulates the immune system response. Without the formation of a complex, most small molecular drugs are unable, alone, to elicit an immunological response. First exposure to the offending drug produces a latent reaction, subsequent exposures usually results in heightened and rapid immunological response. These allergic reactions, characterized by immunohypersensitivity, are most dramatic in anaphylaxis. There are other immune responses that result in adverse reactions or toxicities they include but are not limited to : 1) immune response mediated cytotoxicity which occurs when the drug-protein complex binds to the surface of a cell and this cell-complex is then recognized by circulating antibodies; 2) serum sickness which occurs when immune complexes of drug and antibody are found in the circulation; and 3) lupus syndromes in which the drug or reactive intermediate interact with nuclear material to stimulate the formation of antinuclear antibodies.

In addition to the immune phenomena described above, there are other drug reactions that are syndromes involving allergic reactions. These reactions include, but are not limited to, skin e rashes, drug induced fever, pulmonary reactions, hepatocellular or cholestatic reactions, interstitial nephritis, and lymphadenopathy. Further, there are some drug reactions that mimic allergic reactions but are not immune related. For example, such reactions are due to direct release of mediators by drugs and are called anaphylactoid reactions. An example of this type of adverse event is reaction to radiocontrast dye.

These are common adverse drug reactions that may prevent a candidate therapeutic intervention from use, continued development, and marketing rights. Some of these reactions are reversible, others are not.

Adverse drug reactions include, but are not limited to, the following organs systems: a) hemostasis which encompass blood dyscrasias (feature of over half of all drug-related deaths) which are bone marrow aplasia, granulocytopenia, aplastic anemia, leukopenia, pancytopenia, lymphoid hyperplasia, hemolytic anemia, and thrombocytopenia; b) cutaneous which encompass urticaria, macules, papules, angioedema, morbilliform-maculopapular rash, toxic epidermal necrolysis, erythema multiforme, erythema nodosum, contact dermatitis, vesicles, petechiae, exfoliative dermatitis, fixed drug eruptions, and severe skin rash (Stevens-Johnson syndrome); c) cardiovascular which includes arrhythmias, QT prolongation, cardiomyopathy, hypotension, or hypertension; d) renal which includes glomerulonephritis and tubular necrosis; e) pulmonary which includes asthma, acute pneumonitis,

eosinophilic pneumonitis, fibrotic and pleural reactions, and interstitial fibrosis; f) hepatic which includes steatosis, hepatocellular damage and cholestasis; g) systemic which includes anaphylaxis, vasculitis, fever, lupus erythematosus syndrome; and h) the central nervous system which includes tinnitus and dizziness, acute dystonic reactions, parkinsonian syndrome, coma, convulsions, depression and psychosis, and respiratory depression.

In the cases whereby severe, fatal reactions occur after drug administration, there may be a warning label in the product insert.

For example, tricyclic antidepressants can cause central nervous system depression, seizures, respiratory arrest, cardiac arrhythmias and arrest. The mechanism for the injury is a result of the increased synaptic concentrations of biogenic amines and inhibition of postsynaptic receptors.

Acetaminophen can cause hepatic necrosis as a result of prolonged high dose usage or overdose. In the hepatocyte, acetaminophen is converted to a toxic metabolite that binds to glutathione. As the concentration of acetaminophen increases the levels of glutathione are depleted and the toxic acetaminophen metabolite then binds liver macromolecules. Aggregation of polymorphonuclear neutrophils in hepatic microcirculation may cause ischemia and foster necrotic events.

Halothane can cause hepatic necrosis as well as prodrome fever and jaundice. Interestingly, the liver effects of halothane are usually after a first time exposure. The hepatic reaction is thought to occur via a genetic predisposition to deranged metabolism with the formation of toxic metabolites.

D. Pharmacokinetic Parameters as Potential Mechanisms of Drug-Induced Adverse Reactions Leading to Disease, Disorder, Dysfunction or Toxicities

1. Absorption

Absorption is the pharmacokinetic parameter that describes the rate and extent of the drug, agent, or candidate therapeutic intervention leaves the site of administration. Although absorption is critical for the drug, agent, or candidate therapeutic intervention to ultimately reach the site of physiologic action, the term bioavailability is the parameter that is clinically relevant. Bioavailability is the term used to define the extent to which the active component of the drug, agent, or candidate therapeutic intervention reaches the its site of physiologic action or a biological fluid to which has access to the site of biological action. Although bioavailability is related to all pharmacokinetic parameters, e.g. absorption, distribution, metabolism, and excretion, bioavailability is primarily dependent on the

first ability of the drug, agent, or candidate therapeutic intervention to be absorbed from the site of delivery, i.e. cross cellular membranes.

There are many factors that influence absorption of a drug, agent, or candidate therapeutic intervention. For example, compound solubility, conditions of absorption, and route of administration. In the present invention, we concern ourselves with genes that are involved in the active or passive process of drug, agent, or candidate therapeutic intervention absorption through a biological membrane.

The absorption surface is dependent on the route of administration. For example, absorption of drugs can occur via 1) oral (enteral); 2) sublingual; 3) injections (parenteral, i.e., intravenous, intramuscular, intraarterial, intrathecal, intraperitoneal, or subcutaneous); 4) rectal; 5) inhalation (pulmonary); 6) topical application (skin and eye). In each of these routes of administration, the adsorption rate and extent is dependent on the concentration of the drug at the site, the patency of the epithelial cells, local biological conditions, and function of the active or passive transport.

Absorption can affect both the efficacy and safety of a drug, agent, or candidate therapeutic intervention. For example, for a compound to achieve full pharmacologic potential, it must be available at the target site, be active, and be unbound. In regards to safety, absorption affects safety in one or more of the following: site of delivery pain, necrosis, or irritation; rate of administration; and erratic available concentrations.

2. Distribution

The distribution of the drug, agent, or candidate therapeutic intervention is dependent on the rate and extent the compound enters the bloodstream. Once in the bloodstream, the compound may be distributed to the interstitial and cellular fluids. The distribution of drugs to target tissues can be categorized into two phases. The first distribution phase, is dependent on cardiac output and regional blood flow, both of which are dependent on the health and status of the cardiovascular system. In a second distribution phase, diffusion into tissues is dependent on the level and extent that the drug, agent, or candidate therapeutic intervention is bound. Drug binding by proteins found in the blood can serve to protect the compound from modifications by enzymes, proteins, or compounds in the circulation and or limit the bioavailability of the compound to enter target tissues or individual cells.

Drug entry into tissues requires free drug, and drug binding proteins may limit this active or passive transport. Once distributed into tissues, the drug may be

sequestered within that tissue, to render full pharmacologic activity or to prevent that drug from reaching the appropriate target tissue.

Distribution can affect both the efficacy and safety of a drug, agent, or candidate therapeutic intervention. For example, for a compound to achieve full pharmacologic potential, it must be available at the target site, be active, and be unbound. In regards to safety, distribution affects safety in one or more of the following: distribution to a tissue that is more or less affected by the pharmacologic action of the compound, erratic available concentrations, and tissue specific distribution characteristics.

3. Metabolism

Drugs or xenobiotics, are usually found in the circulation bound to plasma proteins, generally but not exclusive to serum albumin. It is the bound form of the drug that is taken up by the hepatocyte. Bile salts in the circulation are taken up via organic anion transporters. Once inside the hepatocyte, the drug or bile salt is a substrate for a series of reactions that are either oxidative or reductive or reactions that are conjugative steps in the metabolism of the substrate. Generally these chemical modifications are a refined process to render the substrate more hydrophilic, or polar, to be more likely excreted in the bile (via the intestinal tract) or urine (via the kidneys). However, there are exceptions whereby the redox reactions produce reactive intermediates or products that retard elimination. Except for their role in detoxification, there is little in common among the enzymes involved in the redox detoxification reactions. For certain enzymes there are specific groups that will act as substrates, for others there are general classes of chemical compounds that will be suitable substrates for a given enzyme or enzymes.

In the mammalian liver these mechanisms to detoxify and/or enhance the excretion of metabolic by-products, endogenous substrates, and exogenous molecules. The ability to determine whether hepatic function is inadequate is based upon clinical observation, e.g., the presence of jaundice, right upper quadrant abdominal discomfort or pain, pruritis, or by clinical laboratory analyses, e.g., aspartate transaminase (AST or SGOT) or alanine transferase (ALT or SGPT). The hepatic metabolic and excretory mechanisms are critical for short- and long-term survival and are inheritable characteristics. These hepatic biotransformations mechanisms have broad substrate specificity that have been evolutionarily inherited for the host protection from environmental, biological, and chemical substances.

There are two categories of drug, agent, or candidate therapeutic intervention biotransformation (metabolism). In the first, phase I, functionalization reactions occur. Phase I reactions introduce or expose a functional group to the parent

compound. In general, phase I reactions render the parent compound pharmacologically inactive, however there are examples of phase I reaction activation or retention of activity. In phase II reactions, biosynthetic reactions occur. Phase II conjugation reactions leads to a covalent linkage between a functional group on the parent compound with glucuronic acid, sulfate, glutathione, amino acids, or acetate. The metabolic conversion of drugs is the liver, however, all tissues have enzymatic activity.

Factors affecting drug biotransformation are 1) induction of metabolizing enzymes, 2) inhibition of enzymatic reactions, and 3) genetic polymorphisms. It is the interplay of these factors and the health and well being of the patient or subject that determines the fate of parent drug molecules in the body.

The first factor affecting drug biotransformation is induction of metabolizing enzyme activity. The metabolic processes that modify drugs or chemicals (oxidation, reduction, or conjugation) can be induced to significant enzymatic activity. Under physiological conditions, the induction process is in place to coordinately metabolize excess substrates. The induction process can be both at the level of enzymatic activity and increased protein levels of the pertinent enzyme or enzymes. Induction may include one or several of the enzymatic pathways or processes in response to the presence of drugs, xenobiotics, endogenous substrates, or metabolic by-products. There may or may not be increased toxicity as a result of increased concentrations of metabolites. Further, induction of phase I reactive processes (oxidation or reduction reactions) may or may not induce the phase II reactive processes (conjugation reactions).

The second factor affecting drug biotransformation is the inhibition of metabolic enzymes. Enzymatic inhibition can occur via 1) competition of two or more substrates for the enzymatic active site, 2) suicide inhibitors, or 3) depletion of required cofactors for the enzymatic pathways or processes in phase I or phase II reactions.

In competitive inhibition, two or more drugs, xenobiotics, or substrates present can interact with the active site of the enzyme. If one drug binds specifically to the enzymatic active site or to an other intracellular regulatory protein molecule, other compounds are blocked from binding and remain unbound. In this case, unmetabolized parent drug or xenobiotic remains in the circulation, potentially for extended periods of time. Competitive inhibition is dependent on the relative specificity of the substrates for the enzymatic active site and the concentration of the drugs or substrates. An example of competitive drug biotransformation inhibition are cimetidine and ketoconazole which inhibit oxidative drug metabolism by forming a tight complex with the heme iron complex of cytochrome P450, and

macrolide antibiotics such as erythromycin and troleandomycin are metabolized to products bind to heme groups on the cytochrome P450 molecules.

In the second case, the inhibition of enzymes involved in the drug biotransformation process may also occur by suicide inactivation. In these cases, the drug or xenobiotic may interact and covalently modify or render inactive the enzyme involved in the metabolic pathway. In this way, the parent drug compound or molecule is not metabolized, nor is it free to interact with another molecule. Examples of suicide inactivators are secobarbital and synthetic steroids (norethindrone or ethinyl estradiol) which bind to cytochrome P450 and destroy the heme portion of the enzyme unit.

In the third case, inhibition of the enzymes involved in the drug biotransformation pathway can also occur by agents or compounds or physiological status that deplete NADPH or other cofactors required for the enzymatic reactions to occur. In the cases of phase I oxidation or reduction, lack of oxygen or NADPH, may reduce the efficiency and activity of a particular enzyme. In phase II reactions, cofactors provide specific groups for the enzymatic covalent modification of the drug or xenobiotic. These phase II cofactors are required for conjugation biotransformation reactions to occur and depletion of these cofactors would be rate limiting.

The third factor that can affect drug biotransformation is genetic polymorphism. Differences among individuals to metabolize drugs have long been known. Observed phenotypic differences, as determined by amount of drug excreted, through polymorphically controlled pathway/s has lead to a generalized classification of slow (poor) metabolizers and fast (rapid or extensive) metabolizers. In general, poor metabolizers are those with impaired metabolism of a drug via a polymorphic pathway have been associated with an increased incidence of adverse effects. In addition, to date all major deficiencies in drug metabolizing activity are inherited as autosomal recessive traits. Fast or rapid metabolizers are those individuals with processes that extensively metabolize a drug via a polymorphic pathway. The fast or rapid metabolizers have been associated with an increased incidence of ineffective treatment. In these individuals active drug is rapidly metabolized to less active or inactive metabolites such that a reassessment of the pharmacokinetic parameters and dosing regimen may require analysis or readjustment, respectively, for appropriate therapy to occur.

The first observed and catalogued genetic polymorphism associated with drug metabolism was described for isoniazid. Isoniazid is a primary drug prescribed for the chemotherapy of tuberculosis. Marked interindividual variation in the elimination of this drug was observed and genetic studies of families revealed that

this variation was genetically controlled. Isoniazid is predominantly metabolized via N-acetylation. In the analysis of the phenotypically distinct individuals, it was shown that slow acetylators were homozygous for a recessive gene and fast acetylators were homozygous or heterozygous for the wild type gene. It has been
5 determined that the incidence of the slow acetylator phenotype is approximately 50% for U.S. caucasians and blacks, 60-70% of Northern Europeans, and 5-10% in Asians. Other drugs have been shown to be polymorphically acetylated, e.g. sulfonamides (sulfadiazine, sulfamethazine, sulfapyridine, sulfameridine, and sulfadoxine), aminogluthethimide, amonafide, amrinone, dapsone, dipyrone,
10 endralazine, hydralazine, prizidilol, and procainamide. Other drugs that first undergo metabolism and then polymorphically acetylated are clonazepam and caffeine.

Another common genetic polymorphism associated with oxidative metabolism is exemplified by the drug debrisoquine (a sympatholytic
15 antihypertensive). It was discovered that variable inter-patient hypotensive response was due to differing metabolic rates of debrisoquine 4-hydroxylase. Further analysis of family studies revealed that oxidative metabolic reactions are under monogenic control. A cytochrome P450 enzyme, CYP2D6, was determined to be the target gene for debrisoquine 4-hydroxylase activity. Poor metabolizers of debrisoquine
20 are homozygous for a recessive CYP2D6 allele and rapid or fast metabolizers are homozygous or heterozygous for the wild type CYP2D6 allele. Urinary metabolic ratio can be determined after administration of a probe drug and phenotypic assignments (poor or extensive metabolizer) can be identified. The extent of debrisoquine metabolic analysis achieved clinical importance as it was determined
25 that other drugs were poorly metabolized in individuals that poorly metabolized debrisoquine. For example, anti-arrhythmics such as flecainide, propafenone, and mexiletine; antidepressants such as amitriptyline, clomipramine, desipramine, fluoxetine, imipramine, maprotiline, mianserin, paroxetine, and nortriptyline; neuroleptics such as haloperidol, perphenazine, and thioridazine; antianginals such
30 as perhexilene; opioids such as dextromethorphan and codeine; and amphetamines such as methylenedioxymethamphetamine. Further, many β -adrenergic antagonists are metabolized and are subject to polymorphic influence in elimination patterns.

Another example of a genetic polymorphism affecting oxidative metabolism was described for mephenytoin, a drug prescribed for epilepsy. It was shown that a
35 deficiency in the 4'-hydroxylation of S-mephenytoin is inherited as an autosomal recessive trait. The other main metabolic pathway, N-methylation of R-mephenytoin to 5-phenyl-5-ethylhydantoin remains unaffected. Individuals with poor metabolic rate of mephenytoin are subject to adverse central effects, i.e.

sedation. Other drugs can be grouped into the poor mephenytoin metabolizers are mephobarbital, hexobarbital, side-chain oxidization of propranolol, the demethylation of imipramine, and the metabolism of diazepam and desmethyldiazepam. Further analysis of other drugs such as the metabolism of antidepressant drugs (citalopram),
5 the proton pump inhibitor omeprazol, the antimalarial drugs pantoprazole and lansoprazole cosegregate with mephenytoin metabolites.

Because the majority of metabolic enzymes for the conduct of drug biotransformation occurs in the liver, impairment of liver function as a result of hepatic pathological conditions or other disease states can lead to alterations of
10 hepatic or other organ metabolic drug biotransformation. Liver disease pathologies such as hepatitis, alcoholic liver disease, fatty liver disease, biliary cirrhosis, and hepatocarcinomas can impair function of normal physiological metabolic pathways. Further, decreases in hepatic circulation as a result of cardiac insufficiency, hypertension, vascular obstruction, or vascular insult can affect the rate and extent of
15 drug biotransformation. For example drugs with a high hepatocyte extraction ratio would have different metabolism rates affected by alterations of hepatic circulation. Changes in liver blood flow can affect the rate and extent of the metabolism and the clearance of the parent drug. In all cases of hepatic pathological conditions, the affect on drug biotransformation and clearance of parent drugs or metabolized
20 products will be dependent on the severity and extent of the liver organ and hepatocellular damage.

Although hepatic damage may affect the metabolism and clearance of a parent drug or metabolic by-product, residual concentrations of parent drug or metabolic by-products may be deleterious to the liver and its metabolic functions.
25 Following nonparenteral (enteral) administration of a drug, a significant portion of the drug will be metabolized by intestinal or hepatic enzymes before it reaches the general circulation. This first pass effect may generate active drug (administered drug was a prodrug), inactive drug, or toxic drug. Prior to circulation of the metabolized product, circulation to the kidney, the major organ for excretion of the
30 hydrophilic moiety, and excretion via the urine will occur. Therefore, a metabolic product of hepatic metabolic pathways can affect the liver, kidney, and other organs of the body prior to excretion.

a. Phase I Drug Biotransformation: Oxidation and Reduction Reactions

Enzymatic Oxidation of Drugs

In oxidative metabolism, oxidases catalyze the transfer of electrons from substrate to oxygen, generating either hydrogen peroxide or superoxide anions. There are two oxidases present in hepatocytes; they are aldehyde oxidases and

monoamine oxidases. Both of these enzymes have broad substrate specificity and contribute broadly to the metabolism of drugs. A third oxidase, xanthine oxidase, may contribute to the oxidation of drugs, due its ability to catalyze the oxidation of heterocyclic aromatic amines, for example methotrexate and 6-mercaptopurine.

5 Xanthine oxidase in intact tissues is present as a NAD-dependent dehydrogenase, and is converted to an oxidase when there is disruption of the tissue, for example during hepatic cellular damage.

Aldehyde oxidase catalyzes the oxidation of fatty aldehydes to carboxylic acids and the hydroxylation of substituted pyridines, pyrimidines, purines, and pteridines. Generally, xenobiotic aromatic nitrogen heterocycles are metabolized by this enzyme.

Monoamine oxidase is present in two forms, A and B. They are dimeric proteins consisting of identical subunits and FAD is covalently linked to the protein through a cysteinyl residue. Catalytic cycles of monoamine oxidases A or B occur in discrete steps that take an amine and convert it to an aldehyde, while in the process creating hydrogen peroxide and ammonia. These oxidases have a broad specificity; they protect mitochondrial proteins from xenobiotic amines and hydrazines. Further neurotransmitters are metabolized through this route, e.g. serotonin, dopamine, and catecholamines. Primary alkylamines containing unsubstituted methylene group or groups adjacent to the nitrogen exhibits activity. Activity increases as the length of a side chain, with optimal side length being C6. These enzymes also catalyze the oxidation of secondary and tertiary amines and acyclic amines. Hydrazines can be oxidized by these oxidases. Substrates for monoamine oxidases include but are not exclusive to the following amines: benzylamine, dopamine, tyramine, epinephrine, N-methylbenzylamine, and N,N-dimethylbenzylamine; and the following hydrazines: procarbazine 1,2-dimethylhydrazine.

Mono-oxygenases are present in liver cell homogenates and contain two distinct types of xenobiotic mono-oxygenases. They are the cytochrome P450 and the flavin-dependent mono-oxygenases.

The liver microsomal P-450 system consists of a flavoprotein, and a family of related, but distinct, hemoproteins. The flavoprotein catalyzes the transfer of the electrons from NADPH to the hemoprotein, and is the mono-oxygenase. The reaction also requires phosphatidylcholine. The reductase is a monomeric flavoprotein that contains both FAD and FMN. The reductase is specific for NADPH as a reductant, but other oxidants can be substituted. In addition to cytochrome P-450, the flavoprotein catalyzes reduction of quinones, nitro, and azo compounds.

There are many P450 gene families. Subsequent cloning and sequence determination has afforded the ability to divide this gene family into three main groups, CYP1, CYP2, and CYP3, that are responsible for the majority of drug biotransformation. There are further subdivisions in each of these families, examples being CYP2D6, CYP3A4, CYP2E1, as well as others.

Examples of enzymatic inductive processes that affect biotransformation reactions involve the P450 gene family. Specifically, glucocorticoids and anticonvulsants induce CYP3A4; isoniazid, acetone, and chronic ethanol consumption for CYP2E1. Many inducers of the cytochrome P450 enzymes also induce conjugation metabolic enzymes, e.g. glucuronosyltransferases.

In contrast to the monooxygenases, multiple forms of the terminal oxidase (P-450) are present in the hepatocyte. There are many distinct isoforms characterized in different species including humans. It should be noted that mitochondrial P-450 exhibit little or no activity in the metabolism of drugs, xenobiotics, biological compounds, or chemicals. Representative functional groups oxidated by the microsomal P-450 system are as follows: alkanes (hexane, decane, hexadecane); alkenes (vinyl chloride, aflatoxin-B1, dieldrin); aromatic hydrocarbons (naphthylene, bromobenzene, benzo(a)pyrene, biphenyl); aliphatic amines (aminopyrine, benzphetamine, ethylmorphine); heterocyclic amines (3-acetylpyridine, 4,4'-bipyridine, quinoline); amides (N-acetylamino fluorene, urethane); ethers (indemethacin, pheancetin, p-nitroanisole); and sulfides (chloropromazine, thioanisole).

There are many P450s that have been identified in human liver. Substrate specificities vary among these P-450 dependent mono-oxygenases. For example, P4501A1 prefers polycyclic aromatic hydrocarbons; P-4501A2 prefers arylamines, arylamides; P-450A26 prefers coumarin, 7-ethoxycoumarin; P-450 2C8, 2C9, 2C10 prefers tolbutamide, hexobarbital; P-450 2C18 prefers mephenytoin; P-450 mp-1, mp-2 prefers debrisoquine and related amines; P450 2E1 prefers ethanol, N-nitrosoalkylamines, vinyl monomers; P-450 3A3, 3A4, 3A5, 3A7 prefers dihydropyridines, cyclosporin, lovastatin, aflatoxins.

The effect of genetic polymorphism of the P450s has been known for some time. For example, debrisoquine and related drugs; alfentanil, tolbutamide; (S)mephenytoin. Because the P450s can be induced by xenobiotics, an enhanced metabolic rate or efficiency can lead to one drug affecting the potency, efficacy, dosing of another. For example, women taking rifampicin or barbiturates can lead to metabolic inactivation of synthetic oral contraceptives.

The flavin-containing mono-oxygenases are the principle enzymes catalyzing the N-oxidation of tertiary amine drugs to N-oxides. The N-oxides are found in

abundance in serum. Although isoforms have been identified and the catalytic cycle is similar to the cytochrome P450 system, flavin-containing mono-oxygenases substrate specificity differs. Unlike the other flavin-bearing mono-oxygenases, these flavin-containing mono-oxygenases are present in the cell as very reactive oxygen-activated form. It is believed that particular protein structure stabilizes the nucleophilic molecule. Since the molecule is so highly reactive, precise substrate-to-enzyme fit is unnecessary. The following lists substrate types and examples oxidized by the flavin-containing mono-oxygenases: tertiary amines (trifluoperazine, bromopheniramine, morphine, nicotine, pargyline); secondary amines (desipramine, methamphetamine, propranolol); hydrazines (1,1-demethylhydrazine, N-aminopiperidine, 1-methyl-1-phenylhydrazine); thiols and disulfides (dithiothreitol, β -mercaptomethanol, thiophenol); thiocarbamides (thiourea, methimazole, propylthiouracil); sulfides (dimethylsulfide, sulindac sulfide).

Examples of drugs that undergo oxidative reactions are: N-dealkylation (imipramine, diazepam, codeine, erythromycin, morphine, tamoxifen, theophylline); O-dealkylation (codeine, indomethacin, dextromethorphan); aliphatic hydroxylation (tolbutamide, ibuprofen, pentobarbital, meprobamate, cyclosporin, midazolam); aromatic hydroxylation (phenytoin, phenobarbital, propranolol, phenylbutazone, ethinyl estradiol); N-oxidation (chlorpheniramine, dapsone); S-oxidation (cimetidine, chlorpromazine, thioridazine); deamination (diazepam, amphetamine).

b. Enzymatic Reduction of Drugs

The reductases are a class of enzymes that are involved in the metabolic reduction of xenobiotics. This class of enzymes includes the aldehyde and ketone reductases, the quinone reductases, the nitro and nitroso reductases, the azoreductases, the N-oxide reductases, and the sulfoxide reductases. These classes of enzymes are involved in sequential one-electron reduction of some functional groups and produce radicals that can produce damage cellular components directly or indirectly.

The dehydrogenases consist of alcohol dehydrogenases, aldehyde dehydrogenases, or dihydrodiol dehydrogenases. This class of enzymes is involved in the catalysis of hydrogen transfer to a hydrogen acceptor, usually a pyridine nucleotide.

c. Hydrolysis of Drugs

Alternative reactions of detoxification and metabolism of drugs and xenobiotics are initial steps of hydrolysis. Esters, amides, imides, or other

functional groups that are generated as a result of a hydrolysis reaction can alter the hydrophilicity of a molecule and enhance urinary excretion. Hydrolysis occurs both enzymatically and nonenzymatically. Hydrolysis of proteins before they are degraded has been suggested as a step in the process of the aging of intracellular proteins. Antibodies with an affinity for certain esters and certain proteases e.g. 3-phosphoglyceraldehyde dehydrogenase and carbonic anhydrase, have been shown to have esterase activity.

Enzymatic hydrolysis of drugs and xenobiotics include the following enzymes: esterases, amidases, imidases, and epoxide hydratases. Examples of drugs undergoing hydrolysis reactions are: procaine, aspirin, clofibrate, lidocaine, procainamide, indomethacin.

Other hydrolytic processes include reactions owing to both enzymes in tissues, circulation, and those elaborated by microorganisms in the lower bowel; for example, sulfatases, glucuronidases, and phosphatases.

b. Phase II Drug Biotransformation: Conjugation Reactions

In addition, to the redox reactions of the hepatocyte to detoxify or metabolize xenobiotics, there are a series of conjugation reactions. The substrates for these reactions are generally the products from the redox reactions described above. These conjugation reactions involve donation of a suitable hydrophilic molecular group to an accepting xenobiotic or its metabolite. The major function of these covalent modifications is to render the parent compound pharmacologically inactive. The covalent addition of such a group to a parent drug or compound not only inactivates the substrate but also renders the recipient molecule more polar and is more readily excreted via the bile ducts into the intestinal tract or via the urine.

Lipophilic compounds that have one of the functional groups that can serve as an acceptor undergo enzymatic catalysis with a second, donor substrate. The conjugation reactions include the following broad categories: glucuronidation, sulfation, methylation, N-acetylation, and conjugation with amino acids. The enzymes involved in these reactions are as follows: UDP-glucuronyltransferase, alcohol sulfotransferase, amine N-sulfotransferase, phenol sulfotransferase, glutathione transferase, catechol O-methyltransferase, amine N-methyltransferase, histamine N-methyltransferase, thiol S-methyltransferase, benzoyl-CoA glycine acyltransferase, acetyltransacetylase, cysteine S-conjugate N-acetyltransferase, cysteine S-conjugate N-acetyltransferase, cysteine conjugate β -lyase, thioltransferase, and rhodanese. Each of these enzymes has donor and acceptor specificities. The importance of these reactions in the detoxification and metabolism of drugs and xenobiotics are discussed in the examples

Examples of drugs that are known to be conjugated are: glucuronidation (acetaminophen, morphine, diazepam); sulfation (acetaminophen, steroids, methyldopa); acetylation (sulfonamides, isoniazid, dapsone, clonazepam).

5 4. Excretion

Excretion of parent drugs and metabolites can occur in the excretory organs, namely the kidneys, liver, lungs, skin, and breasts (milk). The kidneys are the most important organs for the excretion of drugs and metabolites. Renal excretion involves glomerular filtration, active tubular absorption, and passive tubule
10 reabsorption. The more hydrophilic the compound is the more readily excreted via urine. In addition, many drugs and metabolites are excreted via the bile into the intestinal tract. These metabolites may be excreted in the feces, or may be reabsorbed by the gastrointestinal epithelial cell lining. Organic anions and cations, steroids, fatty acids, and other drugs may be specifically transported into the bile
15 canniculus.

In all of the metabolism and excretion routes, the physiologic goal is to detoxify and rid the body of drugs, xenobiotics, endogenous or exogenous chemicals, or compounds that may or may not be deleterious to the major organs of the body. In principle the detoxification mechanisms function to attain this goal,
20 however there are many cases of major organ toxicity upon exposure to drugs or metabolites of drugs. Although drugs and drug metabolites predominantly affect the liver and kidneys due to the circulatory and physiological processes, other organs can be affected. In the present invention, we address specific genes that may have polymorphic sites affecting metabolic rates to ultimately affect these major organ
25 functions.

a. Excretion of Drugs and Drug Metabolites via the Bile

After parent drugs or xenobiotics are metabolized by redox and or conjugation reactions, the modified products can then be actively transported into
30 the bile cannicula. The transport occurs in an energy dependent fashion requiring ATP. It has been shown that the transporters involved in the active transport from the basolateral (sinusoidal) to the apical (canalicular) surfaces of hepatocytes are members of the ATP binding cassette (ABC) family. The transmembrane electrical potential required to maintain the chemical and electrical potentials required for this
35 active transport is provided by the Na^+/K^+ ATPases located on the basolateral membrane. Other ion transporters are the potassium channel, sodium-bicarbonate symporter, chloride-bicarbonate anion exchanger, and the chloride channel. In the cholangiocyte there are other ion transporters, for example chloride-bicarbonate

anion exchanger, isoform 2, and other organic-solute transporters. Bile acids, phosphatidyl choline, organic anions, organic cations, and cholesterol are actively transported. Approximately 5% of the transporters is multi-drug resistance protein 1 (MDR1) and the remaining are the phospholipid transporter multi-drug resistance protein 3 (MDR3), alicular multispecific organic- anion transporter (multi-drug resistance associated protein (MRP2 or cMOAT), canalicular bile-salt-export pump (BSEP or SPGP(sister of p-glycoprotein)), sodium-taurocholate cotransporter, organic anion-transporting polypeptide, glutathione transporter, and a chloride-bicarbonate anion exchanger are also involved in the transport.

These transporters have been identified to move specific molecules or compounds across biological membranes. For example, the MDR1 protein mediates the canicular excretion of bulky lipophilic cations, e.g. anticancer drugs, calcium channel blockers, cyclosporine A, and various other drugs. In contrast, the MDR3 protein transports phosphatidyl choline from the inner leaflet to the outer leaflet of the canicular membrane. Phosphatidyl choline then can be selectively extracted by intracanalicular bile salts and secreted into bile as vesicles or mixed micelles. MRP2 is involved in the transport of amphipathic anionic substrates e.g. leukotriene C₄, glutathione-S conjugates, glucuronides (bilirubin diglucuronide and estradiol-17 β -glucuronide), sulfate conjugates, and is responsible for the generation of bile flow independent of bile salts within the bile cannicula. SPGP is the canicular bile salt export pump in the mammalian liver.

The hepatocyte has the ability to recruit the ATP-requiring transporters when faced with excessive metabolites. After synthesis, these transporters are stored in compartments that, in response to cAMP, can be actively moved through the cell to the membrane and fused to the cannicula. The active movement from the intracellular compartment to the membrane requires microtubules, cytoplasmic kinesin, cytoplasmic dynein, and calcium. It has been shown that peptides activate phosphoinositide 3 kinase, and increased turnover of phosphoinositides drives the formation of 3'-phosphoinositol, which can activate the transporter in the membrane and ultimately increases movement to the canicular membrane. Signaling pathways via the activation of rab5 stimulate the active movement of the transporters to the internal compartment.

b. Excretion of Drugs and Drug Metabolites via the Kidney

Excretion of drugs or drug metabolites via the kidney and into the urine involves three processes: 1) glomerular filtration, 2) active tubular secretion, and 3) passive tubular reabsorption. The amount of drug or metabolites entering the tubular lumen is dependent on its fractional plasma protein binding and glomerular filtration

rate. In the proximal renal tubule anions and cations are actively transported by carrier mediated tubular secretion and bases are transported by a separate system that secretes choline, histamine, and other endogenous bases. In the proximal and distal tubules there is passive reabsorption of these molecules. The concentration
5 gradient for back-diffusion is created by sodium and other inorganic ions and water.

E. Inflammatory or Immunological Disease, Disorders, or Dysfunctions

Inflammatory or immunological diseases and clinical symptoms includes diseases and processes such as: arthritis (including rheumatoid arthritis,
10 osteoarthritis, and other degenerative syndromes of the joints), asthma, chronic obstructive pulmonary disease (including bronchitis, bronchiectasis, emphysema and other pulmonary diseases associated with obstruction to air flow), interstitial or restrictive lung diseases, autoimmune disease (including systemic lupus erythematosus, scleroderma and other diseases characterized by autoantibodies),
15 transplantation (often treated with long term immunosuppressive therapy), pain associated with inflammation, psoriasis and other inflammatory skin diseases, atherosclerosis (for which there is strong data supporting the role of inflammatory pathogenetic mechanisms), and hepatitis, among other diseases. One skilled in the art will recognize that there may be overlap between some of the conditions listed.

20 Challenges in treating diseases with a significant inflammatory or immunological component include: (i) limited understanding of the pathophysiologic basis of these diseases and conditions, , (ii) a complex mix of immune/inflammatory mediators operating simultaneously, with the primary (initiating) events often unclear and the relative importance of different mediators unknown, (iii) medical interventions that rarely produce specific effects, or
25 address the underlying pathophysiologic basis of the disease or condition. Thus, medical management of inflammatory or immunologic disorders is empirical in nature, is associated with multiple undesirable side effects, and disease progression is common. Based upon these clinical realities and the difficulties drug developers face in developing new treatments for diseases with an inflammatory or
30 immunologic component, the use of genotypebased stratification to identify populations enriched for responders, nonresponders, and/or those likely to develop undesirable side effects will provide clear commercial and medical benefits. Ultimately medical practitioners and patients will also benefit from an enlarged
35 choice of medicines with superior safety and efficacy when used in conjunction with genetic diagnostic tests.

Inflammation is a complex process that comprises different cellular and physiologic events that can be initiated by tissue injury, by abnormal immune

function, or by a wide variety of other endogenous or exogenous factors, not all of which are understood. The inflammatory process can also escape normal regulatory control and become part of the disease process.

Autoimmunity is one aspect of some diseases associated with abnormal immunologic function. Such diseases are characterized by the presence of autoantibodies and oligoclonal B cell populations. Immunological reactions associated with loss of self tolerance may be localized to a specific tissue, or may be systemic. Ultimately, in severe cases, the immune system produces life threatening damage to tissues, physiological function is compromised. Autoimmunity can be initiated by a variety of endogenous (genetic predisposition and others) and exogenous (chemicals, drugs, microorganisms, and others) factors.

F. Endocrine and Metabolic Diseases

The treatment of endocrine and metabolic diseases presents a challenge to physicians and other medical practitioners because the available therapeutics are only partially effective in only a fraction of patients (e.g. antiobesity medications). Further, many currently used medicines produce serious adverse effects (e.g. long term corticosteroid therapy). Therapeutic benefits and toxic side effects have to be balanced in each patient. This requires much attention to drug selection, dosage adjustment and monitoring for potential adverse events on the part of patients and care givers. These limitations of therapy are especially true for the most debilitating endocrine and metabolic diseases such as diabetes and obesity

Difficulties in treating endocrine and metabolic diseases are attributable to factors such as limited understanding of disease pathophysiology, lack of specificity of pathophysiologic changes (e.g. different pathophysiologic mechanisms in patients with similar clinical presentation) and lack of specificity of therapeutic compounds. Further, most medical therapy is directed to the amelioration of symptoms or other secondary changes (e.g. achieving effective control of blood sugar), not the arrest or reversal of underlying pathophysiologic processes. One good example of the difficulty of developing and marketing effective treatments for metabolic and endocrine diseases is the recent history of obesity therapeutics. Only a few products have been approved for treatment of obesity in the United States, and one of them, the anorectic agent dexfenfluramine (d-FF; Redux), a 5-HT reuptake inhibitor and releasing agent, was withdrawn from marketing due to safety problems (pulmonary hypertension, valvular heart disease). Further, a recently marketed antiobesity product (sibutramine; Meridia) with a similar mechanism of action Sibutramine, an inhibitor of serotonin and noradrenaline uptake, reduces appetite (inhibition of serotonin and noradrenaline uptake, reducing appetite) is used by only a small

fraction of eligible obese patients because anti-obesity drugs now have a reputation among caregivers and patients as unsafe. Thus approved drugs for the treatment of a disorder that affects many million Americans are only moderately commercially successful because their shortcomings are widely recognized.

5 In summary, medical management of endocrine and metabolic diseases is empirical in nature, is only partially effective, and is associated with multiple undesirable side effects. In view of these clinical realities, the use of genetic tests to identify treatment responders, nonresponders, and/or those likely to develop undesirable side effects will have a major impact on use of existing classes of drugs
10 for treatment of endocrine and metabolic diseases, as well as on the development and use of new drugs to treat these diseases.

G.Cardiovascular and Renal Diseases

15 The treatment of cardiovascular and renal diseases presents a challenge to physicians and other medical practitioners because the available therapeutics are only partially effective in only a fraction of patients. Further, many currently used medicines produce serious adverse effects. Therapeutic benefits and toxic side effects have to be balanced in each patient. This requires much attention to drug selection, dosage adjustment and monitoring for potential adverse events on the part
20 of care givers – in many cases (e.g. antihypertensive therapeutics) effectively a new pharmacokinetic and pharmacodynamic study must be performed for each patient. These limitations of therapy are especially true of the most debilitating cardiovascular and renal diseases. Although these diseases have distinct clinical presentations, there is extensive overlap in pathogenetic mechanisms and symptoms.

25 Difficulties in treating cardiovascular and renal diseases are attributable to factors such as limited understanding of disease pathophysiology, lack of specificity of pathophysiologic changes (i.e. variation in pathophysiologic mechanisms in patients with similar clinical presentation) and lack of specificity of therapeutic compounds. Further, most medical therapy is directed to the amelioration of
30 symptoms, not the arrest or reversal of underlying pathophysiologic processes.

In summary, medical management of cardiovascular and renal diseases is empirical in nature, is only partially effective, and is associated with multiple undesirable side effects. In view of these clinical realities, the use of genetic tests to identify treatment responders, nonresponders, and/or those likely to develop
35 undesirable side effects will have a major impact on use of existing classes of cardiovascular and renal drugs, as well as on the development and use of new drugs to treat diseases of the cardiovascular and renal systems.

H. Neoplastic Diseases

The unifying feature of neoplastic disease is uncontrolled proliferation and the bulk of modern chemotherapy targets the rapid growth of cancerous tissue. Effective cancer management must destroy or retard the growth of cancerous tissue and prevent the spread of cancerous cells to secondary locations while sparing normal tissues. Cancer therapy has remarkable parallels to the treatment of parasitic infection in that the causative agent is capable of overwhelming growth and rapid mutation to resistant forms. Cancers can differ greatly in their response to chemotherapy: tumors that proliferate rapidly including melanomas, leukemias, and myelomas tend to respond well to classical chemotherapy using cytotoxic agents; tumors that grow slowly, in contrast, such as lung and colon carcinomas tend to respond poorly; the growth of endocrine tumors such as ones of pancreatic, prostate, testicular, ovarian, adrenal, pituitary, or breast origin can be hormonally dependent and treatment with agonists of insulin, estrogen, progesterone, testosterone, etc. function can prove valuable; and solid tumors are more apt to respond to treatment with antiangiogenesis agents than fluid tumors. Surgery (for solid tumors) and radiation treatment exist as therapies that are often used in conjunction with chemotherapeutic agents. A clinician must select a therapy (often a combination of agents and including radiation treatment or surgery) based on tumor type in addition to evaluating the possible toxicities associated with proposed therapeutic regimens, taking the patients current hepatic, renal and myeloproliferative function into account. Since current practice utilizes high doses of cytotoxic agents to minimize the formation of metastases as well as the appearance of secondary, resistant neoplasms, avoiding toxicity becomes a serious issue given the narrow therapeutic index of most drugs in this category.

Medical management of neoplastic disease is empirical in nature, is associated with severe undesirable side effects, and disease progression is common. Based upon these clinical realities and the difficulties medical practitioners face in therapy of neoplastic disease, drug development based upon genotype to identify responders, nonresponders, and or those likely to develop undesirable side effects will be an undeniable beneficial addition to current medical practice.

II. Identification of interpatient variation in response; identification of genes and variances relevant to drug action; development of diagnostic tests; and use of variance status to determine treatment

Development of therapeutics in man follows a course from compound

discovery and analysis in a laboratory (preclinical development) to testing the candidate therapeutic intervention in human subjects (clinical development). The preclinical development of candidate therapeutic interventions for use in the treatment of human diseases, disorders, or conditions begins at the discovery stage
5 whereby a candidate therapy is tested *in vitro* to achieve a desired biochemical alteration of a biochemical or physiological event. If successful, the candidate is generally tested in animals to determine toxicity, adsorption, distribution, metabolism and excretion in a living species. Occasionally, there are available animal models that mimic human diseases, disorders, and conditions in which
10 testing the candidate therapeutic intervention can provide supportive data to warrant proceeding to test the compound in humans. It is widely recognized that preclinical data is imperfect in predicting response to a compound in man. Both safety and efficacy have to ultimately be demonstrated in humans. Therefore, given economic constraints, and considering the complexities of human clinical trials, any technical
15 advance that increases the likelihood of successfully developing and registering a compound, or getting new indications for a compound, or marketing a compound successfully against competing compounds or treatment regimens, will find immediate use. Indeed, there has been much written about the potential of pharmacogenetics to change the practice of medicine. In this application we provide
20 descriptions of the methods one skilled in the art would use to advance compounds through clinical trials using genetic stratification as a tool to circumvent some of the difficulties typically encountered in clinical development, such as poor efficacy or toxicity. We also provide specific genes, variation in which may account for interpatient variation in treatment response, and further we provide specific
25 exemplary variances in those genes that may account for variation in treatment response.

The study of sequence variation in genes that mediate and modulate the action of drugs may provide advances at virtually all stages of drug development. For example, identification of amino acid variances in a drug target during
30 preclinical development would allow development of non-allele selective agents. During early clinical development, knowledge of variation in a gene related to drug action could be used to design a clinical trial parameters in which the variances are taken account of by, for example, including secondary endpoints that incorporate an analysis of response rates in genetic subgroups. In later stages of clinical
35 development the goal might be to first establish retrospectively whether a particular problem, such as liver toxicity, can be understood in terms of genetic subgroups, and thereby controlled using a genetic test to screen patients. Thus genetic analysis of drug response can aid successful development of therapeutic products at any stage of

clinical development. Even after a compound has achieved regulatory approval its commercialization can be aided by the methods of this invention, for example by allowing identification of genetically defined responder subgroups in new indications (for which approval in the entire disease population could not be achieved) or by providing the basis for a marketing campaign that highlights the superior efficacy and/or safety of a compound coupled with a genetic test to identify preferential responders. Thus the methods of this invention will provide medical, economic and marketing advantages for products, and over the longer term increase therapeutic alternatives for patients.

There are some examples whereby there is no direct evidence that a gene or genes are involved in drug response of a candidate therapeutic intervention. In these cases, however, there is genetic data supporting a role of a variance or variances involved in the etiology, progression, or risk of the neurologic or psychiatric disease. These cases, including but not limited to anxiety, Huntington's disease, demyelinating disease, pain, Parkinson's disease, spasticity, and stroke are described below with details of current therapies and potential genetic involvement of variances in drug responses.

Neurological and Psychiatric Diseases

There are some examples whereby there is no direct evidence that a gene or genes are involved in drug response of a candidate therapeutic intervention for the treatment of neurological or psychiatric disease. In these cases, however, there is genetic data supporting a role of a variance or variances involved in the etiology, progression, or risk of the neurologic or psychiatric disease. These cases, including but not limited to anxiety, Huntington's disease, demyelinating disease, pain, Parkinson's disease, spasticity, and stroke are described below with details of current therapies and potential genetic involvement of variances in drug responses.

A. Anxiety

Description of Anxiety

Anxiety is a common, nonspecific symptom associated to a greater or lesser degree with many psychiatric diseases, including psychoses, neuroses, mood disorders and personality disorders. It is also an inevitable component of everyday life brought on by stressful events such as medical or surgical procedures. Some prominent nonspecific symptoms of anxiety include tachycardia, chest pains, or irregular heartbeat; epigastric distress; headache, dizziness, syncope, or paresthesias. It is usually some combination of these physical manifestations of anxiety that impels patients to seek medical care. It has been estimated that approximately 13% of primary care visits are substantially attributable to anxiety.

There are both acute and chronic anxiety syndromes. The acute forms include panic attacks and event-related anxiety. Chronic, or generalized anxiety is a pervasive feeling of nervousness that does not subside. Because both panic-attack and generalized anxiety lead to desire for being alone or away from public places, many patients adopt agoraphobic tendencies. These patients can become housebound because of fear of having a panic attack in a public setting.

Current Therapies for Anxiety

The principal treatments for anxiety have been benzodiazepines, monoamine oxidase inhibitors, antidepressants, and β -adrenergic antagonists. In all cases, both panic attack and generalized anxiety, concurrent continued behavioral and psychological therapy is required to regain a sense of normal life function.

Limitations of Current Therapies for Anxiety

The difficulty in determining the efficacy of psychotropic drugs for the treatment of anxiety is the subjective contribution of the nonpharmacologic factors that are associated with anxiety. However, the relative safety of benzodiazepines, pharmacologic actions, and high demand make these products drugs of choice in the treatment of anxiety.

The benzodiazepines are associated with side effects due to CNS depression, drowsiness and ataxia. Other side effects are: increase in hostility or irritability, confusion, weight gain, skin rash, nausea, headache, impairment of sexual function, vertigo, and lightheadedness.

Future Drug Development for Anxiety

In Tables 2, 13 and 19, there are listings of candidate genes and specific single nucleotide polymorphisms that may be critical for the identification and stratification of a patient population diagnosed with anxiety based upon genotype. Current pathways that have possible involvement in the therapeutic benefit of anxiety include, but are not limited to, serotonergic, GABAergic, purinergic, adrenergic, glutaminergic, dopaminergic, cholinergic, glycinergic, cholecystokinin, corticotropin releasing factor, histaminergic, opiate, taurine, oxytocin, neuropeptide Y, estrogen, hemostasis, tachykinin, vasopressinergic and second messenger intracellular cascades gene pathways that are listed in Tables 2, 13 and 19. One skilled in the art would be able to identify these pathway specific gene or genes that may be involved in the manifestation of anxiety, are likely candidate targets for novel therapeutic approaches, or are involved in mediating patient population differences in drug response to therapies for anxiety.

Below, Table 26 lists the therapies in development for anxiety categorized by the gene pathway mechanism of action as in Table 7. The listed candidate therapeutic interventions response in patients with anxiety may be affected by polymorphisms in genes as described above.

B. Huntington's disease

Description of Huntington's Disease

Huntington's disease (HD) is an inherited disorder characterized by the gradual onset of motor incoordination and cognitive decline in mid-life. Symptoms develop insidiously either as a movement disorder manifested by brief jerk-like movements of the extremities, trunk, face, neck (choreas) or as personality changes. Fine motor incoordination and impairment of rapid eye movements are early features. Bradykinesias and dystonia may predominate if the onset occurs early in life.

As the disorder progresses the involuntary movements become more severe and are characterized by: dysarthria, dysphagia, and impaired balance. Cognitive deficits begin by features of slowed mental processing, difficulty in organizing complex tasks, and memory deficits (family, friends, and immediate situation is unaffected). These patients have tendencies to become irritable, anxious, and clinically depressed. In rare cases there may be paranoia or delusional states. There are approximately 25,000 Americans diagnosed with HD.

Current Therapies of HD

Current therapies do not include alternatives for the treatment of the progression of the neurodegeneration. Medical management of the associated clinical symptoms includes the following categories: depression, psychosis, and choreas. In the cases of depression and psychoses, the therapies of beneficial therapeutic use are described in this invention.

The treatment of choreas generally includes neuroleptic agents that affect dopaminergic pathways by antagonism at the receptor level. Monoamine depleting drugs can also be used to minimize choreas.

Limitations of Current Therapies of HD

Efficacy Limitations

Conventional and atypical neuroleptic agents are not uniformly able to reduce the signs and symptoms of choreas in HD patients. Efficacy varies in the HD population in one or combination of the following ways: 1) patients are only

partially responsive or 2) patients are therapy resistant. Unfortunately, limited efficacy in a HD population in light of the presence of undesirable side effects may lead to compliance issues, aberrant drug abuse behavior, and further safety issues.

Thus, a clinician when presented with a newly diagnosed HD patient, in general, follows standard neurological society or published guidelines for first line therapy. However, when faced with a partially responsive or therapy resistant patient, the clinician can choose from multiple agents, none being completely effective, has limited guidance or rationale to select one agent the other, and follows an empirical medical decision making course of action.

Toxicity Limitations

Unfortunately, conventional neuroleptic drugs are uniformly, and atypical are latently, associated with undesirable dose-dependent side effects. These include but are not exclusive to sedation, weight gain, cognitive deficits, sexual or reproductive insufficiencies, agranulocytosis, cardiovascular complications, neuroleptic malignant syndrome (parkinsonism with catatonia), jaundice, blood dyscrasias, skin reactions, epithelial keratopathy, seizures, and extrapyramidal effects. The blood dyscrasias include mild leukocytosis, leukopenia, and eosinophilia. The skin reactions include urticaria and dermatitis and are usually associated with phenothiazines. Epithelial keratopathy and opacities in the cornea is associated with chlorpromazine therapy. In extreme cases these effects may impair vision. These ocular deposits tend to spontaneously disappear upon discontinuation of chlorpromazine drug therapy.

The extrapyramidal side effects of conventional neuroleptics include dystonia (facial grimacing, torticollis, oculogyric crisis), akathisia (feeling of distress or discomfort leading to restlessness or constant movement), and parkinsonian syndrome (rigidity and tremor at rest, flat facial expression). With long term usage of conventional neuroleptic drugs, tardive dyskinesias uniformly appear in HD patients.

Tardive dyskinesia is a syndrome of repetitive, painless, involuntary movements. These abnormal involuntary movements are insuppressible, stereotyped, autonomic movements that cease only during sleep, vary in intensity over time, and are dependent on the level of arousal or emotional distress. The syndrome is characterized by quick choreiform (ticlike) movements of the face, eyelids (blinks or spasms), mouth (grimaces), tongue, extremities, or trunk. These movements may have varying degrees of athetosis (twisting movements) and sustained dystonic postures. Increasing the dose of the conventional neuroleptic

agent can reverse extrapyramidal effects observed in patients. However, increasing the dose ultimately leads to more severe dyskinesias. Antiparkinson agents tend to exacerbate the tardive dyskinesia symptoms and thus are not used clinically.

Because dopaminergic agonists tend to worsen the symptoms and dopaminergic antagonists tend to retard the symptoms of tardive dyskinesias, the optimal alternative is to use a neuroleptic agent that has selective dopaminergic antagonist activity. This alternative therapy would manage both psychosis and dyskinesias.

Often a clinician faces the dilemma of a patient with medically managed choreas, but the dose-related tardive dyskinesias, agranulocytosis, or seizures compels the medical care personnel to opt to switch therapies to possibly those agents or drugs with fewer or less severe side effects but with substandard or limited efficacy. Under these conditions, inability to treat the psychotic or chorea symptoms with the backdrop of irreversible dyskinesias leaves the patient with few alternatives.

III. *Impact of Genotyping on Drug Development for HD*

There have been reports of polymorphisms in key genes that affect neuroleptic activity in schizophrenic patients. These polymorphisms may be further applicable for neuroleptic response in HD patients. For example, within the dopamine D4 receptor subtype, there are known tandem repeats in exon 3. In a recent study, schizophrenic patients on maintenance doses of chlorpromazine were stratified into two groups, one having 2 tandem base pair repeats and the other having 4 tandem base pair repeats. Thirty-four percent of group one patients and 62% of group two patients had a favorable response to chlorpromazine therapy during acute stage treatments. The presence of homogeneous four 48 base pair repeats in both alleles in exon 3 of the dopamine D4 receptor subtype thus appears to be associated with beneficial chlorpromazine response.

Recently, a study of the serotonin receptor subtype 6, polymorphism (T267T vs. C267T) in a group of patients refractory to clozapine therapy was reported. In this study, it appeared that the T267T genotype patients were more likely to respond to continued therapy than those patients with C267T genotype patients.

A recent report documented a correlation of the serotonin 5HTC2 receptor subtype biallelic polymorphism and neuroleptic efficacy. A significant number of schizophrenic patients homozygous for the allele C2 responded unsatisfactorily to antipsychotic medication as compared to control.

Three polymorphisms in the serotonergic receptors, i.e. 5HT2A (T102C); 5HT2C (cys23ser); and 5HT2A (his452tyr) have reports of positive or negative correlation with efficacy of antipsychotic therapies. This disparity in the literature

will, in the future, be further examined in schizophrenic patient populations and correlation may be discovered.

V. Description of Mechanism of Action Hypotheses for Future Drug Development

5 The genetic basis of the disease has been identified. A gene, huntingtin, whose protein has a mechanism yet to be defined, has a series of CAG tandem repeats. The number of CAG repeats do correlate somewhat with age of onset and the severity of the disease. Cell death starts in the caudate nucleus by an unknown mechanism. The huntingtin protein is essential to life. The huntingtin protein
10 undergoes cleavage as cells age. The mechanism of cleavage is performed in part by members of the caspase enzymatic family. As the huntingtin protein is cleaved into smaller units, the peptides become toxic, and it has been shown that the smaller fragments tend to migrate into the nuclear compartment. It has been shown that preventing huntingtin cleavage prevents cellular toxicity. Some of the cleaved
15 huntingin fragments form aggregates which may promote or be a by-product of neuronal cell death.

 The profound loss of neurons in the brains of patients with HD has lead to many development programs for the promotion of neural regeneration. These programs broadly include cytokines, growth factors, and agents that promote neural
20 or glial cell growth. Further, consideration of preventing neuronal cell death includes apoptosis inhibition and others. Other programs include prevention of prolonged excitatory neurotransmission. These neurons switch their aerobic metabolism to anaerobic metabolism leading to glycolytic metabolism and excessive production of lactate and metabolic by-products. Excitatory neural inhibition,
25 improvement of energy metabolism, and inhibition of cell death signals may ultimately play a critical role in preventing, retarding, or halting neurodegeneration in HD patients.

 Further, there may be genes within pathways that are either involved in metabolism of neurotransmitters or are involved in metabolism of various drugs or
30 compounds. In Tables 1-6, 12-17, 18-23, there are listings of candidate genes and specific single nucleotide polymorphisms that may be critical for the identification and stratification of a patient population diagnosed with HD based upon genotype. Current pathways that may have involvement in the therapeutic benefit of HD include glutaminergic, serotonergic, dopaminergic, cholinergic, opiates, estrogen,
35 mitochondrial maintenance, growth, differentiation, and apoptosis. secretion gene pathways that are listed in Tables 2, 7, 13, and 19. One skilled in the art would be able to identify these pathway specific gene or genes that may be involved in the manifestation of HD, are likely candidate targets for novel therapeutic approaches,

or are involved in mediating patient population differences in drug response to therapies for HD.

Below in 30 is a list of therapies in development for HD categorized by the gene pathway mechanism of action. The listed candidate therapeutic interventions
5 response in patients with HD may be affected by polymorphisms in genes as described above.

C. The Demyelinating Diseases

Description of Demyelinating disease

Primary demyelinating diseases result in loss of the myelin sheath that
10 surrounds axons, with preservation of the axons. The main demyelinating diseases are multiple sclerosis, including its variants (Marburg and Balo variants of MS and neuromyelitis optica), and the perivenous encephalitides, which include acute disseminated encephalomyelitis and acute necrotizing hemorrhagic leukoencephalitis..

15 Due to the paucity of information concerning etiology of these diseases, identification and classification is largely descriptive. The most common and best studied of these diseases is multiple sclerosis.

Description of Multiple Sclerosis

20 Clinically, MS usually starts as a relapsing illness with episodes of neurological dysfunction lasting several weeks, followed by substantial or complete improvement. This is the relapsing-remitting phase of the disease. Many patients remain in this stage of the disease for years or even decades, while others rapidly progress to the next stage, secondary progressive MS, in which, with repeated
25 relapses, recovery becomes less and less complete. There is also a steadily progressive relapse-independent form of the disease termed primary progressive MS. This form is characterized by a steady worsening of neurological function without any recovery or improvement, and more often affects men.

30 Current Therapies for Multiple Sclerosis

Although the pathogenesis of MS is not understood, there is accumulating evidence that immunoregulatory mechanisms are involved. Current therapy of MS is therefore directed to modulating immune function and thereby halting or retarding myelin degeneration, or facilitating remyelination. Remyelination has been shown
35 to occur spontaneously in response to therapeutic interventions in animals (both normals and MS models). However, in MS animal models remyelination appears to be aborted soon after it begins.

For relapsing-remitting MS the following agents are currently in use : 1) interferon beta-1 β (Betaseron) reduces annual relapse rate and reduces development and progression of new lesions in relapsing-remitting MS as monitored by magnetic resonance imaging (MRI), and has been shown to reduce annual relapse rate, reduce disability progression, and delay increase of lesion volume by MRI in secondary progressive MS; 2) Interferon beta-1 α (IFN-beta-1 α ; Avonex) treatment results in reduced disability progression, annual relapse rate, and new brain lesions, as visualized by MRI; 3) Glatiramer acetate (Copaxone; Copolymer-1; Cop-1) reduces annual relapse rate; 4) Intravenous immunoglobulin, reduces annual relapse rate, and delays disability progression; 5) High-dose methylprednisolone therapy is effective in shortening MS attacks, and may be useful in the long term treatment of secondary-progressive MS; 6) Other agents that have been used with success are mitoxantrone, azathioprine and methotrexate. The latter drug, in particular, has been shown effective in reducing disease activity, both by decreasing the number of exacerbations and by slowing clinical progression. The first four agents are of comparable efficacy in the treatment of relapsing-remitting MS. Not enough trials have been performed to reliably assess the utility of treating nonresponders to one of these treatments with a different treatment, or to assess potential markers of response.

III. Limitations of Current Therapies for Multiple Sclerosis

The available treatments have both efficacy and toxicity limitations. Further, the cost for one year of interferon treatment is approximately \$11,000 and parenteral administration is inconvenient.

Partial Response to Therapy

Current therapies reduce, but do not arrest, disease progression, and only a fraction of patients benefit from treatment; approximately 30% of patients on interferons experience reductions in relapse rates. For primary progressive MS, there are currently no effective therapies available; interferon beta-1b has in fact been shown to worsen spasticity in primary progressive MS.

Undesired Side-Effects or Toxicities as a Therapeutic Limitation

All interferons are associated to varying degrees with flu-like symptoms, muscle-ache, fever, chills, and asthenia. There are also side effects that are difficult to distinguish from the course of the demyelinating illness, for example interferons may lower the seizure threshold and exacerbate depressive illnesses, two clinical problems also observed in patients without interferon therapy.

Impact of Pharmacogenomics on Drug Development for Multiple Sclerosis

Aspects of therapy for demyelinating disease that can be addressed by pharmacogenetic methods include: 1) Which patients are most likely to respond to medication? 2) Which drugs are most likely to benefit which patients? 3) What is the optimal dose and duration of treatment? 4) What is the relationship between disease type, stage and manifestations and drug response? 5) Can adverse treatment responses be predicted? As an alternative to directly correlating genetic variants with clinical responses to therapy, one could also use quantitative biochemical, immunological or anatomical measures of disease activity to assess the impact of genetic variation in candidate genes on response to medication. While it is unlikely that all therapeutic responses are under strong genetic control, it is expected that if stratification based upon genotype were performed in clinical trials a correlation between drug response and genotype will be detected for at least some treatment responses. Described below and in Tables 2 and 7 are gene pathways that affect current drug therapy as well as drugs currently in development for MS. Described in the Detailed Description are methods for the identification of candidate genes and gene pathways, patient stratification, clinical trial design and statistical analysis and genotyping for testing the impact of genetic variation on treatment response in multiple sclerosis and other demyelinating diseases.

A sample of therapies approved or in development for preventing or treating the progression of symptoms of MS currently known in the art is shown in Table 32. In this table, the candidate therapeutics were sorted and listed by mechanism of action. Further, the product name, the pharmacologic mechanism of action, chemical name (if specified), and the indication is listed as well.

Mechanism of Action Hypotheses for Novel Therapies for Multiple Sclerosis: Utility of Genotyping

Several possible mechanisms by which intravenous immune globulin (IVIG) modulates the course of the disease are related to limiting the inflammatory process and repairing the damage by enhancing remyelination. The efficacy of dexamethasone (DX) and methylprednisolone (MP) at high (HD) and low (LD) dose in acute multiple sclerosis (MS) relapses was evaluated by a double-blind trial in 31 patients followed for 1 year. DX and HDMP were similarly efficacious in promoting recovery, while LDMP was ineffective in the short-term outcome and was followed by an early clinical reactivation. The different outcomes seem to be related to different immunomodulating effects, mainly on cerebrospinal fluid (CSF) IgG

synthesis and on peripheral blood and CSF CD4+ lymphocyte subsets. The efficacy of interferon should be investigated in relation to other treatment options, such as immunoglobulin, copolymer I, azathioprine and methotrexate. Other promising therapeutic options (mitoxantrone, intravenous immunoglobulins, drug associations) are under evaluation.

Pathogenesis of MS

There are three current theories for the cause of MS that have been studied to effectively understand the mechanism of disease as well as establish rationale for the development of effective candidate therapeutic interventions. The three current theories are 1) viral infection, 2) genetic predisposition, 3) inflammation and autoimmunity, and 4) ion channel modulators.

Viral Infection

Indirect evidence that there is a single unique virus causing MS is the unusual geographic distribution of the disease. There is a documented north-south gradient of disease prevalence, migration studies, and reports of clustering of cases have indicated an environmental influence on disease susceptibility. Despite years of intense research including viral isolation studies from tissue samples of MS patients and controls, has not resulted in identification of an MS specific virus or viral sequence.

One virus implicated in the pathogenesis of MS is the human herpes virus type 6 (HHV-6). HHV-6 is a neurotropic virus that can establish a latent infection in man. HHV-6 protein and DNA have been isolated and identified from neuroglial cells in active MS spinal lesions. Further, HHV-6 IgM titers in MS patients and HHV-6 DNA identified in serum samples indicate a recent infection. However, to date there is no evidence that HHV-6 is the causal infectious agent of MS. Instead, a hypothesis of molecular mimicry has been proposed as a likely possibility to explain the indirect immune-mediated injury to otherwise normal tissue in the course of clearing an infectious agent. Besides HHV-6, there are other neuro-specific infectious agents that may damage the CNS through this mechanism. The molecular similarity (mimicry) between virus and myelin antigens may be permissive for immunological cross-reactivity between HHV-6 and myelin antigens. In this model, the T-cells become activated, cross the blood brain barrier and misidentify normal myelin antigens as 'virus' resulting in T-cell mediated cellular and tissue injury.

Genetic Susceptibility to MS

Although MS is a sporadic disease, studies have pointed to an organized familial clustering, which suggests a genetic predisposition to MS. Equally likely, these studies also suggest that there is a genetic predisposition to an environmental stress or causal event.

The most convincing evidence of a genetic predisposition to MS is derived from studies of a population-based study of twins. The risk of MS increases with the degree of shared information within a family. There is further a marked increase in concordance for MS in the comparison of monozygotic and dizygotic twins.

Inflammation and Autoimmunity in MS

While it is clear there is an inflammatory component to the lesions of MS, is it currently unclear whether the immune system plays a role in initiation of the characteristic damage of white matter.

In experimental studies of animal models of MS, there appears to be T-cell, CD4+ and CD+8, autoreactivity to several putative CNS antigens including myelin basic protein, proteolipid protein, myelin oligodendroglial glycoprotein, 2',3'-cyclic nucleotide phosphodiesterases, myelin-associated glycoproteins, and viral antigens. Further, there appears to be down regulation of cytokine production including TNF- α and IL-3.

These observations have led to the following proposed mechanism of immune-mediated injury in an MS lesion. Genetic and environmental factors (e.g. viral infection, molecular mimicry, bacterial lipopolysaccharides, superantigens, local metabolic stress, oncogene expression, or reactive metabolites) may potentiate the movement of T-cells through the blood-brain barrier to the CNS. These same genetic and environmental factors may act within the CNS to upregulate the expression of intracellular adhesion molecules on endothelial cells and the circulating T-cells which in turn enhances the rolling, binding, diapedesis, and ultimate migration of the T-cells into the CNS. The same genetic and environmental factors may activate the secretion of $\alpha\beta$ -crystallin on the oligodendrocytes rendering these cells more susceptible to T cell recognition. The T-cells once in the CNS then secrete cytokines (TNF- β and INF- γ) activate the antigen presenting cells (astrocytes, microglia, and macrophages) enhancing (macrophage, microglia) or inhibiting (astrocytes) further immune signaling. The activated T cell then encounters the putative MS antigen or antigens in light of the MHC class II molecules on the antigen presenting cells, resulting in T-cell activation. The activated T-cells can then differentiated into Th1 or Th2 type CD4+ cells which then results in proinflammatory or anti-inflammatory cytokine signaling, respectively. It

has been shown in MS patients that antibody, complement, and antibody-mediated cellular toxicity mechanisms may cause the myelin lesions.

Ion Channel Modulations in MS

Reduction of the depolarization in postsynaptic membranes by modulation of the ion channels in nerve and muscle tissue has been postulated as a mechanism to ablate aberrant neurotransmission in demyelinating neurological disease. Proposed gene targets to produce the membrane depolarization are the nicotinic acetylcholine receptor, voltage gated Na⁺ channels, and other ion channels.

Future Therapeutic Strategies for MS

The future strategies for the beneficial therapy of MS are borne out of the existing mechanisms of the etiology of this demyelinating disease as previously described. They are antivirals, cytokine and anticytokine strategies, immune deviation strategies to enhance Th2 cell/cytokine performance, matrix metalloproteinase inhibitors, trimolecular complex strategies, cathepsin B inhibitors, and oxygen radical scavengers.

Specifically, antivirals include valcyclovir and acyclovir. Cytokine and anticytokine strategies include TNF inhibitors, antiinflammatory cytokines, and inhibitors of proinflammatory cytokines. Immune-deviation strategies to enhance Th2 cell/cytokine predominance includes pentoxifylline, transforming growth factor- β (TGF- β), and Il-10, Il-4 alone in combination with corticosteroids. Matrix metalloproteinase inhibitors include D-penicillamine, and hydroxymatate. Trimolecular complex strategies include anti-MHC monoclonal antibodies, MHC class II hypervariable peptide vaccines, anti-T cell monoclonal antibodies, altered peptide ligands, T cell vaccination strategies (myelin basic protein reactive T-cell, T-cell receptor peptide vaccination), co-stimulation strategies (anti-7-1, CTLA-4Ig fusion proteins, CD40/CD40 ligand interactions), and adhesion molecule signaling strategies (monoclonal antibodies, or small molecules directed to these adhesion molecules).

Neural regeneration development programs will include growth factors including NGF, BDGF, CNTF, NT-3, and other cytokines, as well as other factors that are involved in the support of nerve cell viability, growth, and sustaining neural transmission.

Technological advances that reduce difficulties in determining progression of the demyelination by neuroimaging techniques will aid development of new therapies. Estimation of expected clinical and surrogate measures and patterns to

identify, screen, and develop statistically derived stopping rules for efficacy and futility.

Further, there may be genes within pathways that are either involved in metabolism of neurotransmitters or are involved in metabolism of various drugs or compounds. In Tables 2, 13, 19 there are listings of candidate genes and specific single nucleotide polymorphisms that may be critical for the identification and stratification of a patient population diagnosed with MS based upon genotype. Current pathways that may have involvement in the therapeutic benefit of epilepsy include glutaminergic, GABAergic, opiates, corticotropin releasing hormone, potassium channel, prostaglandin, platelet activating factor, cytokines, clot formation, second messenger cascade, growth, differentiation, and apoptosis, cytoskeleton, adhesion, and myelination gene pathways that are listed in Tables 2, 7, 13, and 19. One skilled in the art would be able to identify these pathway specific gene or genes that may be involved in the manifestation of MS, are likely candidate targets for novel therapeutic approaches, or are involved in mediating patient population differences in drug response to therapies for MS.

D. Pain

Description of Pain

Chronic pain can be caused by chronic pathologic processes in somatic structures or viscera, or by prolonged dysfunction of parts the peripheral or central nervous system.. In all there are approximately 70 million Americans that experience chronic pain. Chronic pain may be the result of recurrent headache, arthritis, back or spinal injuries, musculoskeletal disorders, cardiac or visceral pathologies. Chronic pain is also part of the clinical manifestation of cancer; many of these cases are medically intractable pain. Chronic pain syndromes include polyarteritis nodosa; systemic lupus erythmatosus; entrapment neuropathy; lumbar plexitis; Bell's palsy; carpal tunnel syndrome. Chronic pain can also result from peripheral neuropathies: diabetic neuropathy (neuropathic complications of diabetes mellitus include distal symmetric, sensory, autonomic, asymmetric proximal, cranial and other mononeuropathies); cervical radiculopathy; Guillain-Barre syndrome; brachial plexitis; familial amyloid neuropathy; HIV neuropathy; post spinal cord injury; and post herpetic neuralgia.

Current therapies for Pain

Therapeutic management of chronic pain includes a three step ladder approach: non-opioid analgesics are stepwise prescribed in combination with moderate to potent opiates. The guidelines call for a determination by the patient

and the physician of pain relief. Broadly speaking, the guidelines are as follows: mild pain is treated with non-opioid analgesics, moderate or persisting pain is treated with a weak opioid plus non-opioid analgesics, and severe pain that persists or increases is treated with a potent opioid plus non-opioid analgesics.

5 Pain management regimens include not only the use of opioids and non-opioid analgesics, but also benzodiazepines, local anesthetics, anticonvulsants, anticholinergics, serotonin norepinephrine reuptake inhibitors, neuroleptics, and barbiturates. These drugs in combination can relieve associated symptoms of chronic pain syndromes such as anxiety, acute on top of chronic pain, seizures, dry
10 mouth, delirium, and inability to sleep, respectively.

Treatment options for chronic pain fall into the following categories: 1) general health promotion and relief from exacerbating factors; 2) nonnarcotic pharmacologic; 3) physical; 4) surgical; and 5) narcotic.

15 The nonnarcotic empirical therapies include tricyclic antidepressants (amitriptyline, nortriptyline, doxepin, imipramine), anticonvulsants (carbamazepine, phenytoin); GABAergic agonists (BACLOFEN[®]) and antipsychotics (fluphenazine). Narcotic therapies include opioid agonists (methadone and fentanyl). Devices and surgical therapies can be used in combination with drug therapy. In general these therapies have been shown to reduce pain and each are described in detail below.

20 Antidepressants: The tertiary amines are the most commonly used anti-depressants to manage pain associated with post-SCI. Although the exact mechanism is unknown, the interference with the re-uptake of neurotransmitters (dopamine, norepinephrine, and serotonin) may reduce pain transmission in the afferent
25 pathways. Further, the increased quantities of these neurotransmitters in the areas of the hyperexcitable neurons, descending pain inhibitory pathways that terminate in the substantia gelatinosa of the dorsal horn, may act to reduce pain transmission. Interestingly, the dose of the tricyclics for the management of pain is approximately half that required for the management of depression. These compounds can be
30 determined to be effective for pain management in approximately two weeks.

Anticonvulsants: Reports exist describing chronic neuropathic pain syndromes as a central neurophysiologic epileptiform activity of the uncontrolled hyperactive neurons leading to a convulsive syndrome in the spinal cord. Thus, anticonvulsant
35 therapies are considered to stabilize the threshold against hyperexcitability of neurons and inhibiting the spread of epileptiform activity in neurons involved in nociception. Further, activation of inhibitory neurons may lead to a pain reduction.

Although the data is not conclusive, it appears that anticonvulsants are more effective when given in combination with antidepressants.

5 Neuroleptics: The neuroleptics are thought to exert a potentiation of the antidepressants and may impart a dopaminergic antagonism. Neuroleptics are usually given in combination with an antidepressant.

10 GABAergic agonists: Baclofen, a GABAergic agonist when delivered intrathecally was effective in reducing chronic pain in those patients in which the pain was of musculoskeletal origin (83% of these patients), but was ineffective in those patients with neurogenic pain (78% experienced no change).

15 Physical treatments: Physical treatments include transcutaneous electrical nerve stimulation (TENS) and spinal cord stimulation devices. Using TENS, some success has been reported to reduce peripheral pain. Upon placing the electrodes, peripheral sensory nerve stimulation is thought to activate pain inhibitory interneurons in the substantia gelatinosa or dorsal root entry zone of the spinal cord. Spinal cord stimulation devices are programmable multichannel systems with electrodes that may be placed percutaneously, these systems do not require
20 laminectomy. These stimulators have been shown to reduce chronic pain (perceived pain levels requiring intensive therapies: discomforting, distressing, horrible, and excruciating) by 50% long term. The global ratings for quality of life in these patients demonstrated similar long term improvements. The exact mechanism of how spinal cord stimulation results in a reduction of pain is unknown, but it is
25 thought to occur through an antisympathetic effect. Further, it seems to be effective in cases in which the patient has neuropathic or an ischemic component to the pain. In patients with peripheral neuropathies (postherpetic neuralgia, intercostal neuralgia, causalgic pain, diabetic neuropathy, idiopathic neuropathy) spinal cord stimulation is able to reduce chronic pain in approximately 50% of the patients.

30 Surgical treatment: If conservative pharmacologic approaches have failed to relieve pain, neurosurgery can be considered. Neurosurgical treatments consist of nerve blocks, neuroablative and neuroaugmentative procedures.

35 Nerve blocks: Peripheral, epidural, and sympathetic nerve blocks have been attempted. However, the analgesic effect is usually short-lived and ineffective against central mechanisms of pain.

Neuroablative procedures: There are surgical procedures that are rarely performed because they have been shown to be ineffective, i.e. sympathectomies, neurolyses, dorsal rhizotomies, cordectomies, anterolateral cordectomies, mesencephalotomies, and cingulotomies. These procedures have been superseded by dorsal root entry zone (DREZ) surgery. The surgical procedure involves a laminectomy of the appropriate vertebrae, examination of the DREZ and radiofrequency lesions of the DREZ. The mechanism of this ablative surgery is thought to be due to the destruction of the secondary pain sensory neurons in the substantia gelatinosa in the dorsal horn. Success of this procedure on the reduction of pain has been reported at 60-90%.

Neuroaugmentative procedures- deep brain stimulation: Electrodes are implanted in the periventricular gray matter, specific sensory thalamic nuclei, or the internal capsule.

Limitations of Current Therapies of Pain Due to Low Efficacy

The severity of pain can be debilitating and significantly interfere with the productivity and quality of life. Existing therapies for chronic pain are often inadequate and characterized by the tendency to become ineffective with time. Potent opiates are part of an analgesic regimen, however, dose-limiting side effects and antinociceptive capacity, tolerance and potential for dependence limit their widespread use. Surgical intervention is sometimes attempted, but often such procedures are ineffective and at best provide only temporary relief.

There are many syndromes by which the above combination drug therapy is insufficient to relief symptoms of chronic pain. There are common reasons for unrelieved pain associated with the patient or family, i.e. belief that pain in cancer is inevitable and untreatable, failure to contact a physician, patient denial, failure to take medications, noncompliance due to fear of addiction, noncompliance due to a belief that tolerance will rapidly develop and adequate pain relief then will not be available in the advanced stages, and lastly noncompliance due to the adverse side effects. Common reasons for unrelieved pain associated with the physician or nurse are: denial of the patient's pain, unawareness of pain intensity, failure to perceive patient denial, failure to treat pain aggressively, fear of patient addiction, failure to prescribe appropriate doses for analgesia, failure to monitor the patient's progress, failure to understand alternative drug combinations, and finally failure to give psychological support to the patient and family. Despite these common reasons for unrelieved chronic pain, even under positive conditions chronic pain can be intractable in a variety of diseases.

The coexistence of pain and depression in these patients is a dependent relationship, i.e. when the pain is unmanaged the depression becomes more severe, the reverse (increased depression leads to increased pain) relationship is less likely to occur. The characteristic intensity of the pain and psychological impact prompts extreme potential solutions. Some of these pain syndromes are more resistant to analgesic therapy, for example approximately half of the individuals with spinal cord injuries endure chronic pain and 30% experience severe, debilitating chronic pain. Approximately 75% of advanced stage cancer patients experience moderate to severe pain and approximately half of these individuals are refractory to standard therapy for management of pain.

Other efficacy limitations include: slow onset of symptoms (2-3 weeks) before efficacy detection for tricyclic antidepressants.

Limitations of Current Therapies of Pain Due to Toxicity or Undesired side effects

In the stepwise approach to therapy, physicians are able to monitor and adjust the doses to limit undesired side effects of opioids: sedation, cognitive impairment, myoclonus, addiction, and respiratory depression. Further, opiate tolerance is a well documented effect seen in routine narcotic users and abusers. These side effects may provoke a use of opioid rotation in a pain management schedule.

Although the use of opioids in acute and chronic cancer associated pain is well accepted, their use in chronic noncancer pain has been widely considered to be inappropriate due to concerns over efficacy, toxicity and addiction.

Other unwanted or undesirable side effects include tardive dyskinesias limit the use of neuroleptics in the management of chronic pain; oral baclofen is associated with drowsiness and confusion. Further, baclofen may cause hepatotoxicity. Complications of radiofrequency lesions of DREZ procedure includes cerebrospinal fluid leaking, loss of sensory/motor functions, exacerbation of bowel, bladder, or sexual dysfunction, and epidural/subcutaneous hematomas. Patients must consider the risks of this procedure, particularly the potential loss of two levels of sensation. Associated with deep brain stimulation are complications due to the release of large amounts of natural opioids leading to deafferentation and nociceptive pain.

Impact of Genotyping on Drug Development for Pain

As described above, there is evidence to suggest that there are efficacy and safety differences to drug therapy in the pain patient population. Although not all of these responses may be attributable to genotypic differences, it is expected that if

stratification based upon genotype were performed, a reasonable correlation between drug response and genotype may become obvious. As described below, there are gene pathways that are involved with current drug therapy and those that may be potentially involved in the future. As described in the Detailed Description, methods for the identification of candidate genes and gene pathways, stratification, clinical trial design, and implementation of genotyping for appropriate medical management of a given disease is easily translated for pain syndromes. As described below in section V. below there are likely gene pathways as are those that are outlined in the gene pathway Table 2 and CNS matrix table 7.

For example, optimization of GABAergic, opiate, or ion channel modulation mediated therapy of pain further demonstrates the utility of selection of a potential epilepsy patient that has a predisposing genotype in which selective analgesics or agents are more effective and or are more safe. In considering an optimization protocol, one could potentially predetermine variance or variances within the GABAergic receptor, ion channel or ion channel mediated mechanisms of neurotransmission, or GABAergic receptor mediated intracellular mechanism of action that is preeminently responsible for drug response. By embarking on the previously described gene pathway approach, it is technically feasible to determine the relevant genes within such a targeted drug development program for pain.

A sample of therapies approved or in development for preventing or treating the progression of symptoms of pain currently known in the art is shown in Table 33. In this table, the candidate therapeutics were sorted and listed by mechanism of action. Further, the product name, the pharmacologic mechanism of action, chemical name (if specified), and the indication is listed as well.

Description of Mechanism of Action Hypotheses for Future Drug Development for Pain

The persistence of pain most likely involves a cascade of pathological neurochemical events that lead to abnormal sensory hyperexcitability and excitotoxicity. The persistence of hyperexcitability involves a sequence of neuroplastic events in the spinal cord. In particular, the hyperexcitability cascade involves NMDA receptor mediated intracellular calcium-dependent increase of nitric oxide (NO) and cGMP production. These signals facilitate long-term alterations in neuronal excitability and central sensitization. The altered spinal neurochemical environment results in an impairment of neural inhibitory function. In particular, inhibitory gamma-aminobutyric acid (GABA)-ergic interneurons are susceptible to excessive excitatory amino acid release. Recent studies suggest that abnormal pain sensations may be alleviated by application of GABA receptor

agonists. The analgesic capacity of GABA receptor agonists has been demonstrated in numerous animal models of acute and chronic pain.

Further, there may be genes within pathways that are either involved in metabolism of neurotransmitters or are involved in metabolism of various drugs or compounds. In Tables 2, 13, and 19, there are listings of candidate genes and specific single nucleotide polymorphisms that may be critical for the identification and stratification of a patient population diagnosed with pain based upon genotype. Current pathways that may have involvement in the therapeutic benefit of epilepsy include glutaminergic, serotonergic, dopaminergic, adrenergic, cholinergic, histaminergic, purinergic, GABAergic, glycinergic, melatonin, nitric oxide, peptide protein hormone processing, opiates, cholecystokinin, tachykinin, bradykinin, corticotropin releasing hormone, somatostatin, galanin, calcium or sodium channels, prostaglandin, cytokines, growth, differentiation, apoptosis, lipid transport/metabolism pathways that are listed in Tables 2, 7, 13, and 19. One skilled in the art would be able to identify these pathway specific gene or genes that may be involved in the manifestation of pain, are likely candidate targets for novel therapeutic approaches, or are involved in mediating patient population differences in drug response to therapies for pain.

E. Parkinson's Disease

Description of Parkinson's Disease

Parkinson's disease (PD) is one of the major neurodegenerative disorders of middle and old age. PD is a clinical syndrome that is dominated by four clinical symptoms: tremor at rest, bradykinesia, rigidity, and postural instability. There are secondary clinical signs and symptoms also associated with PD and are a result of the following manifestations: mood and intellectual disorder, oculomotor control, and autonomic and sensory dysfunction. PD can be generally categorized by the clinically predominant parkinsonian feature: 1) those patients having tremor, or 2) those patients having postural instability and or gait difficulty as the predominant clinical parkinsonian manifestation. In those patients with tremor predominant disease, the onset is earlier in life and exhibits a slower progression than those patients with gait difficulties or postural instability. In the latter case, the age of onset is later in life and is more frequently associated with bradykinesias, dementia, and the movement disorder progresses more rapidly. The stages of PD have been described and are referred to as Hoehn and Yahr stages I through V; stage I- signs and symptoms are unilateral, stage II- signs and symptoms are bilateral, stage III- signs and symptoms are bilateral and balance is impaired, stage IV- functionally disabled, and stage V- patient is confined to wheelchair or bed.

Resting tremor and bradykinesias are the hallmarks of PD. Bradykinesias are primarily responsible for the altered clinical presentation for most PD patients: retardation of activities of daily living and generalized slowing down of movements, lack of facial expression (hypomimia or masked facies), staring expression due to limited ability to blink, impaired swallowing which causes drooling, hypokinetic and hypophonic dysarthria, monotonous speech, micrographia, impaired simultaneous and repetitive movements, difficulty in standing from a chair and turning in bed, shuffling gait with short steps, decreased arm swing and other autonomic movements, start hesitation and sudden freezing of motion. Freezing of motion manifests as a sudden and often unpredictable inability to move and represents the single most disabling parkinsonian symptoms.

There are several disorders other than PD that manifests with parkinsonian symptoms. For example, acquired or symptomatic parkinsonism is the result of infectious (postencephalitic and slow virus) disease, side effects from drugs (neuroleptics (antipsychotic and antiemetic drugs), reserpine, tertabenazine, amethyl dopa, lithium, flunarizine, cinnarizine), toxins (MPTP, carbon dioxide, manganese, mercury, cesium, methanol and ethanol), cerebrovascular insult (multi-infarct, hypotensive shock), trauma (pugilistic encephalopathy), and others (parathyroid abnormalities, hypothyroidism, hepatocerebral degeneration, cerebral tumors, normal pressure hydrocephalus, syringomesencephalia). Parkinsonism can also be the result of hereditary degenerative disease, for example autosomal Lewy body disease, Huntington's disease, Wilson's disease, Hallervorden-Spatz disease, olivopontocerebellar and spinocerebellar degenerations, familial basal ganglia calcification, familial parkinsonism with peripheral neuropathy, and neuroacanthocytosis. Lastly, parkinsonism can be the result of multiple-system degenerations and include for example progressive supranuclear palsy, Shy-Drager syndrome, striatonigral degeneration, Parkinsonism-dementia-amyotrophic lateral sclerosis complex, corticobasal ganglionic degeneration, Alzheimer's disease, and hemiatrophy-parkinsonism. These non-PD parkinsonism symptoms can be clinically identified as distinct from PD due to the presence of atypical signs or symptoms of the particular dysfunction or syndrome, absence or paucity of tremor, and poor response to levodopa.

Current Therapies for PD

Pathophysiologically, idiopathic PD cases are almost uniformly identified by the absence of dopaminergic terminals and depigmentation within the substantia nigra and the presence of Lewy bodies (eosinophilic cytoplasmic inclusions in neurons consisting of aggregates of normal filaments). These abnormalities are

predominantly found in the ventrolateral region of the substantia nigra which is the region that projects to the putamen. It has been estimated that at least 80% of dopaminergic neuronal loss within the substantia nigra and an equal degree of dopamine depletion within the striatum is required before signs and symptoms of PD is clinically observed.

There are currently four categories of drug therapies for the treatment of PD: dopaminergic replacement drugs, dopaminergic agonists, anticholinergic drugs, and monoamine oxidase inhibitors. Other therapies include surgical treatment and implantable devices for control of debilitating essential tremor.

Dopaminergic Replacement Drugs- therapy of PD is aimed at replacing the lost dopamine that has resulted in the loss of dopaminergic neurons in the substantia nigra and other brain regions. L-dopa is a prodrug that can be converted to dopamine within the existing neurons. Generally, L-dopa is beneficial in early PD, because it is effectively metabolized in presynaptic terminals and secreted in an active form. Due to the rapid decarboxylation of L-dopa in the periphery, administration of large doses is required to achieve therapeutic benefit. However, L-dopa is usually administered with carbidopa, an inhibitor of peripheral decarboxylation and thus greater concentrations of L-dopa enters the CNS. The combination of L-dopa and carbidopa reduces by 75% the amount of L-dopa required.

Dopaminergic Agonists- dopaminergic agonists can be administered in the early stages of the disease, examples include pramipexole and pergolide.

Anticholinergic Drugs- anticholinergic agents are prescribed for the management of tremor or inordinate movements associated with PD, examples include trihexyphenidyl, and benztropine. The majority of the anticholinergic therapies for the adjunct treatment of PD are long-acting medications thus relief of symptoms may continue through the night when patients have difficulty turning in their bed, and to rise in the morning.

Monoamine Oxidase Inhibitors- inhibition of the metabolism of dopamine by monoamine oxidase can be achieved to increase the synaptic levels of dopamine. An example is selegiline.

Others- catechol-o-methyl transferase inhibitors may be prescribed for the adjunctive treatment of PD, example is Tasmar. An antiviral, symmetrel, has been used for the relief of tremors, rigidity, and bradykinesia. Some β -adrenergic antagonists have been shown to reduce tremors, example is propranolol.

Prior to the advent of levodopa therapy, the most effective means of treating disabling tremors associated with PD were thalamotomy and pallidotomy. These ablative surgical procedures are associated with improved tremor and in certain cases, bradykinesias. Recent advances in neurosurgery, e.g. devices to specifically record from the globus pallidus for enhanced localization, have been employed and there is renewed clinical interest in considering these therapies for the treatment of PD. This therapy has the advantage of single procedure therapeutic intervention of disabling tremors.

Another therapeutic alternative for the treatment of essential tremor, a device for deep brain stimulation, is approved for unilateral implantation in the ventral intermediate nucleus of the thalamus. A programmable, implantable pulse generator is implanted just below the clavicle. The implanted device has been shown to be effective in 20% of the patients, bilateral implantation and stimulation is under investigation.

Limitations of Current Therapies for PD

Although there are therapeutic alternatives for the early intervention of PD, there are few alternatives for the later stages and for the side effects that develop after long term therapy. These limitations are discussed below.

Limitations of Current Therapies due to Low Efficacy

All anti-Parkinson drugs have two qualities that limit the efficiency of treatment regimens. First, the drugs are relatively short acting. A single administration does not relieve symptoms for the duration of waking hours, and multiple administrations are required. The second is that these drugs are all centrally acting drugs and starting dosage is low and slowly increased. Abrupt withdrawal or reductions of any of these medications can lead to deleterious side effects.

L-dopa therapy of PD has therapeutic benefit in the early stages of the disease. However, as the movement disorder progresses, the dopaminergic terminals are lost and the prodrug is no longer converted to the active form. The therapeutic benefit is then limited to the level and extent of the intact postsynaptic neurons.

Long-term therapy with levodopa is associated with dose dependent side effects including inefficacy, "on-off" phenomena, and dyskinesias. Response fluctuations occur in approximately 80% of the patients. These fluctuations consist of wearing-off phenomena, a gradual loss of effectiveness of levodopa related to the timing of administration of the drug, and the on-off phenomena, which is an abrupt

loss of the effectiveness of levodopa that is not related to the timing of administration.

Dyskinesias, consisting of chorea and dystonia, occur in approximately 40% of patients treated with levodopa. These dyskinesias are most frequently observed when plasma levels of L-dopa are high. For patients with preexisting history of psychiatric illness, anticholinergic therapies are less likely to be administered and further if prescribed are less likely to be effective. Thalamotomy and pallidotomy are two surgical procedures that can only be performed once per side. Thus, refractory cases or cases whereby surgery was not sufficient to alter the essential tremor, additional surgery is unavailable. Deep brain stimulation is only 20% effective, requires extensive follow-up, and is associated with a surgical morbidity of 5%. Animal model studies of growth factors, GDNF, affected sprouting of peripheral neurons and those in the spinal cord. Unregulated neural sprouting can be deleterious to neurological function.

Limitation of Current Therapies due to Toxicity or Undesired Side Effects

Limitations due to toxicity or undesired side effects for the above discussed treatments of PD are as described below for each of the treatment strategies.

Dopaminergic replacement drugs- as described above, L-dopa is a prodrug that can be of therapeutic benefit to patients with PD. However there are side effects and toxicities associated with L-dopa therapy, they are choreiform and dystonic dyskinesias and other involuntary movements, adverse mental changes such as paranoid ideation, psychotic episodes, depression, and cognitive impairments (dementia). Dyskinesias associated with levodopa, can be debilitating and as uncomfortable as the rigidity and akinesia of PD.

Reductions or withdrawals of L-dopa therapy have been associated with neuroleptic malignant syndrome (NMS). NMS is an uncommon but life-threatening syndrome characterized by fever or hyperthermia, muscle rigidity, involuntary movements, altered consciousness, autonomic dysfunction, tachycardia, tachypnea, sweating, and hyper- or hypotension.

Dopaminergic agonists- as described above, dopaminergic agonists are useful for the activation of post synaptic dopaminergic receptors. The side effects and toxicities associated with dopaminergic agonists are: abnormal involuntary movements, hallucinations, "on-off" phenomena, dizziness, fainting, visual disturbances, ataxia, insomnia, depression, hypotension, constipation, vertigo, and shortness of breath. It

has been observed clinical laboratory transient elevations of blood sera urea and nitrogen, SGOT, SGPT, GGPT, CPK, alkaline phosphatase, and uric acid.

Anticholinergic drugs- the predominant affect afforded by the anticholinergic drugs is to treat the extrapyramidal effects that develop with long-term dopaminergic therapies. This therapy is thus via the anticholinergic and antihistaminergic effects. However, there are adverse reactions that are associated with anticholinergic therapies, they are tachycardia, paralytic ileus, constipation, dry mouth, toxic psychosis (confusion, disorientation, memory impairment, visual hallucinations, possible exacerbation of preexisting psychiatric symptoms or syndromes, blurred vision, dysuria, and urinary retention.

Monoamine oxidase inhibitors- selective inhibition of monoamine oxidase type B (MAO-B) enzyme activity is a useful adjunctive therapy to increase concentrations of dopamine in regions of the brain. Since MAO-B is predominantly found in the brain, fewer systemic side effects occur. Despite this selectivity, there are side effects that are undesirable, they are exacerbation of L-dopa or other dopamine agonist mediated side effects. For example, dyskinesias are enhanced as well as the others listed above.

MAO-B inhibition can be deleterious if administered with a tricyclic antidepressant. Further, a combination of MAO-B inhibitor and meperidine (an opioid narcotic) has lead to stupor, muscle rigidity, severe agitation, and hyperthermia. Thus, concomitant administration of these two types of drugs is avoided.

Others- inhibition of COMT as described above is a useful therapeutic alternative to many PD patients. However, there are associated side effects and toxicities associated with this drug family. In some patients there is a clinical liver enzyme elevation that requires monthly monitoring and liver function tests are routinely administered every 6 weeks for the first three months of therapy. Liver impairment can result in the reduction of drug detoxification mechanisms, and clinically as jaundice.

Because COMT and monoamine oxidase are the two predominant metabolizing enzymes for catecholamines, concurrent therapy of a COMT and a non-selective monoamine oxidase inhibitor may result in aberrant neuroexcitotoxicity. However, selective monoamine oxidase inhibitors of MAO-B may be administered together.

Other side effects include dyskinesias, nausea, sleep disorders, dystonia, excessive dreaming, anorexia, muscle cramps, and orthostatic hypotension.

Surgical treatment and implantable devices- both pallidotomy and thalamotomy are routinely considered for the treatment of refractory essential tremor. The extent and level of surgical success is dependent on accurate localization of the globus pallidus or the thalamus. Surgery that includes either of these two methods is a one attempt procedure, too much surrounding brain tissue may be lost in subsequent procedures. A side effect may be loss of cerebral function in surrounding areas that may or not result in clinical relevant or observable disease.

Impact of Genotyping on Drug Development for PD

For Parkinson's disease, there is evidence to suggest that there are efficacy and safety differences to drug therapy in the PD patient population. Although not all of these responses may be attributable to genotypic differences, it is expected that if stratification based upon genotype were performed, a reasonable correlation between drug response and genotype may become obvious. As described below, there are gene pathways that are involved with current drug therapy and those that may be potentially involved in the future. As described in the Detailed Description, methods for the identification of candidate genes and gene pathways, stratification, clinical trial design, and implementation of genotyping for appropriate medical management of a given disease is easily translated for PD. As described below in section V. below there are likely gene pathways as are those that are outlined in the gene pathway table 2 and the matrix table 7.

Description of Mechanism of Action Hypotheses for Future Drug Development

Motor symptoms of PD result primarily from the degeneration of dopaminergic innervation within the putamen and the caudate nucleus. Further dopaminergic degeneration within the mesocortical and mesolimbic systems may be responsible for the cognitive deficits and neurobehavioral symptoms. Autonomic dysfunction often observed in PD patients may be the result of loss of dopaminergic function in the hypothalamus. Although dopaminergic pathways have been studied extensively in post mortem PD patients loss of neurotransmitter pathways that may be responsible for additional clinical symptomology. For example, loss of noradrenergic innervation in the locus ceruleus may contribute to the sudden and unpredictable freezing of motion and degeneration of cholinergic neurons in cortical areas may lead to observed dementia in PD patients.

There have been recent proposals for the mechanism of selective neuronal cell death and functional loss. The proposed mechanisms involved in the

progressive degeneration of dopaminergic neurons are oxidative stress, mitochondrial dysfunction, excitotoxic damage, cell death. Below each is described, with proposed gene targets.

Oxidative stress: In oxidative stress, generation of reactive oxygen species, part of the normal cellular metabolism, is aberrant and levels exceed the regulated cellular metabolism or scavenging mechanisms. The free radicals are generated by the conversion of superoxide ions to hydrogen peroxide via the enzyme superoxide dismutase and the reaction of hydrogen peroxide with reduced glutathione to produce water under the control of glutathione peroxidase. Since it has been documented a 60% reduction in the available reduced glutathione as well as an increased generation of iron associated with neuromelanin, there is a potential shift in the balance of the capacity to scavenge hydrogen peroxide radicals.

Oxidative stress may also be part of circuitous pathway leading to cell death that is as follows: generated free radicals lead to mitochondrial damage, which leads to neuron excitotoxicity, which leads to increased concentrations of intracellular calcium which increases the generation of free radicals. All four pathways (free radicals, mitochondrial damage, neural excitotoxicity, and increased intracellular calcium) can independently lead to neuron cell death. Neuroprotective agents, antioxidative agents, and those agents having effects of halting, retarding, or preventing progression of neurodegeneration may affect one or more of these pathways leading to therapeutically relevant agents.

Mitochondrial damage: In mitochondrial damage, the evidence is born out of the experiments of the specific neurotoxin, MPTP. MPTP is a protoxin, its active form MPP⁺ has been shown to result from its inhibition of mitochondrial respiration at the level of complex I, the complex that controls the transfer of one electron from NADH to co-enzyme Q and the transfer of two protons to the mitochondrial inner space, both are then used to synthesize ATP from ADP. In addition, MPP⁺ is thought to increase leakage of electrons at complex I, thereby increasing the generation of superoxide. Since the association of MPTP and the evolution of PD in intravenous drug users, it has been shown that there is a decrease in complex I activity in the substantia nigra in PD patients and is relatively unique to PD than other neurodegenerative disorders.

Excitotoxic damage: In excitotoxic damage, the theory posits there is an excess glutaminergic signal from the neocortex and the subthalamic nucleus to the substantia nigra. The excess signal, by acting at NMDA receptors, changes the

permeability of the neural cells to calcium which leads to aberrant post synaptic membrane potentials, enhanced propensity for depolarization and latent repolarization, and activation of nitric oxide synthase (NOS). Activation of NOS leads to the generation of free oxygen radicals through the peroxynitrite reaction.

5 Since the discovery that output neurons of the subthalamic nucleus provide a glutaminergic excitatory input to the substantia nigra, increased calcium influx into the cells and increased formation of nitric oxide via the activation of NOS, may be particularly harmful in PD due to the defect in mitochondrial complex I (see above). Excitotoxic damage to the substantia nigra, thus potentially stems from the integrity

10 of the substantia nigra and or overactivity of the subthalamic nucleus. Thus, strategies aimed at dual actions of enhancing dopaminergic status (dopamine agonism) in the substantia nigra and reducing subthalamic overactivity (glutaminergic antagonism).

Cell Death: In neural cell death, neurons in the substantia nigra undergo death

15 signals via necrosis and apoptosis. In studies involving double labeling with the TUNEL assay (apoptosis) to determine DNA fragmentation and cyanine dye labeling to determine cell structural detail, it was shown that DNA fragmentation and chromatin condensation occurs in the same nuclei of neurons in substantia nigra in patients with PD. Therefore, it appears that the number of apoptotic nuclei in the

20 substantia nigra in PD is greater than that seen in normal aging, consistent with the 10-fold higher rate of cell loss observed in patients with PD. Thus, antiapoptotic agents or therapies may halt, retard, or prevent the progression of neurodegeneration.

Neuroprotection afforded by growth factors in general or specific to neurons

25 have been considered. Growth factors including but not limited to BDNF, GDNF, bFGF have been studied in preclinical animal models of PD. Furthermore, GDNF has been tested in clinical trials.

Alternative neurotrophic agents are a group of ligand called the immunophilins. These ligands have been shown to have neurite growth promoting

30 and neuroprotective effects. Although these effects were first described from results of experiments of the immunosuppressive agents, cyclosporine and FK-506, nonimmunosuppressive analogues have been generated to have neuroprotective capacity while having none of the immunosuppressive qualities. These low molecular weight ligands may hold promise for the medical management of PD.

Based upon these varying hypotheses as stated above, there are many products in development for PD. Table 34 below lists current therapies that are in development for PD.

F. Spasticity

Description of Spasticity

Spasticity is a complication that occurs in patients with diagnosed neurodegenerative diseases or cerebral insults such as multiple sclerosis, cerebral palsy, tetanus, traumatic brain injury, post traumatic spinal cord injury, amyotrophic lateral sclerosis, dystonic syndromes (axial dystonia), and stroke. Together there are approximately 1.8 million individuals with spasticity in the U.S. Spasticity is a term that generally refers to one of a variety of forms of muscle hypertonicity, hyperactive muscle stretch reflexes, exaggerated tendon reflexes, and clonus and flexor spasms. Spasticity is commonly described as an isokinetic movement disorder distinguished by velocity-dependent increase in muscle tone characterized by hyperactive stretch reflexes. Patients with spasticity have impaired voluntary control of skeletal muscles, difficulty relaxing muscles once movement has stopped, difficulty initiating rapid movements, and an inability to regulate controlled movement.

Clinically, there are three types of spasticity 1) mild, characterized by hyperactive reflexes and unsustained myoclonus; 2) moderate, characterized by involuntary, uncontrolled contractions, sustained myoclonus neither of which affects activities of daily living; and 3) marked or severe, characterized by unpredictable, uncontrolled paroxysms of spasm and involuntary clonus; these can throw the patient from a wheelchair and often the patient cannot lie in bed quietly; these patients have difficulties using a wheelchair, and transfers (for example: from bed to chair) are problematic.

Broadly speaking there are two groups of spasticity patients: cerebral origin spasticity (etiologies resulting from congenital or acquired injuries such as trauma (traumatic brain injury), anoxia (cerebral palsy), or stroke); spinal origin spasticity (etiologies include spinal cord injury and multiple sclerosis). Uncontrolled spasticity exacerbates physical disabilities, increases the cost of care, and profoundly impacts the quality of life for the patient and family.

Current Therapies for Spasticity

Mild to moderate spasticity is medically managed with the available treatments. Little to no data are available with respect to waning of efficacy or

progression of the spasticity to more severe forms. With prolonged marked spasticity, contractures (static muscle shortening due to chronic spasm) may develop so that neither lying nor sitting occurs without undue pressure on bony prominences which lead to chronic pressure sores.

As the severity of the spasticity is a continuum, so are the therapies. Spasticity may not require treatment until it becomes painful, bothersome to the patient, or interferes with the activities of daily living. Existing treatments for spasticity may be categorized as systemic or locally acting.

Systemic Oral Medications

These are dantrolene (interferes with the excitation-contraction coupling mechanism by interfering with Ca^{++} (dantirum), baclofen (GABA_B agonist, lioresal), diazepam (GABA agonist, valium), tizanidine hydrochloride (β_2 -agonist, zanaflex). Back-up medication is the α -agonist, clonidine.

Locally Acting Treatments

Locally acting treatments include intrathecal baclofen, surgical or chemical rhizotomy, and nerve motor point blocks.

Intrathecal baclofen

Oral Baclofen is associated with undesirable side effects, however, Baclofen can be delivered to the subarachnoid space attached to a subcutaneous pump. Intrathecal baclofen is a convenient therapy and this form of drug delivery poses fewer central side effects. Further, intrathecal baclofen has shown to reduce spasticity, improve functional capabilities, and increases functional range of passive movement.

Surgical intervention

This category includes rhizotomy, which has been most successful in the treatment of spasticity in children with cerebral palsy. In elderly patients that may have stroke induced spasticity, rhizotomy is uncommon and virtually not considered. Another surgical procedure, tendon lengthening, can be considered in those patients in which the lower extremities are affected. This procedure can be considered in those stroke patients who have developed spasticity.

Chemical Rhizotomy

Chemodenervation is performed via injections of phenol (or ethanol) or botulinum toxin. In phenol injections, there is neurolysis of the motor nerve. This nerve block technique is useful for motor neuron associated spasticity, and is generally avoided in cases where sensory and motor neurons are hyperactive. The improvement of spasticity after phenol injections may last for a few weeks to years.

Botulinum toxin (BTX) injection into motor neurons has proven useful in the treatment of spasticity. This potent neurotoxin isolated from *Clostridium botulinum*, acts by binding to receptors at the neuromuscular junctions. The binding to the type A toxin is highly specific. The deactivation of intracellular presynaptic vesicles to release acetylcholine in the synaptic cleft can re-establish normal muscle tone and contractility. Intramuscular delivery of BTX has the advantages of lack of sensory effects, lack of caustic chemicals such as phenol, ability to target specific muscle groups through the use of electromyography, and an ability to weaken muscles in a graded fashion.

Limitations of Current Therapies for Spasticity: Efficacy and Toxicity Systemic Local Medications

With the exception of dantrolene (which acts directly on muscle), all of the other oral medications act on the central nervous system and there are unwanted effects from the medications, i.e. drowsiness and confusion. Dantrolene and baclofen may cause hepatotoxicity, and dantrolene may cause weakness in other muscle groups. Further, the systemic treatments are highly nonselective. As listed above, there are some indications that these oral medications are less likely to reduce the spasticity; outcomes of oral medications in the treatment of cerebral origin spasticity are poor as compared to good outcomes in patients with spinal origin spasticity. Often combination regimens are used to attempt to curb the myoclonus.

Locally Acting Treatments

Intrathecal Baclofen- The limitations of this method of delivery are numerous: pump failure, infection, catheter migration, and the need to refill the reservoir. The half-life for ITB is 4-5 hours, and the pump must be refilled at least every 90 days.

Chemodenervation this technique is dependent on the proficiency of the surgeon and the accuracy of motor stimulation electromyography (EMG). Phenol injection close to a sensory nerve can result in causalgia due to injury of the myelin sheath of the sensory nerve.

BTX- There are studies that demonstrate a resistance to the toxin, these studies have shown that an antibody titer to the toxin prevents full potency.

Impact of Pharmacogenomics on Drug Development for Spasticity

As described above, there is evidence to suggest that there are efficacy and safety differences to drug therapy in the spasticity patient population. Although not all of these responses may be attributable to genotypic differences, it is expected that if stratification based upon genotype were performed, a reasonable correlation between drug response and genotype may become obvious. As described below, there are gene pathways that are involved with current drug therapy and those that

may be potentially involved in the future. As described in the Detailed Description, methods for the identification of candidate genes and gene pathways, stratification, clinical trial design, and implementation of genotyping for appropriate medical management of a given disease is easily translated for spasticity. As described
5 below in section V. below there are likely gene pathways as are those that are outlined in the gene pathway table, Table 2, and the gene pathway /indication matrix table, Table 7.

Optimization of GABAergic or ion channel modulation mediated therapy of spasticity further demonstrates the utility of selection of a potential spasticity patient
10 that has a predisposing genotype in which selective antispasticity or agents are more effective and or are more safe. In considering an optimization protocol, one could potentially predetermine variance or variances within the GABAergic receptor, ion channel or ion channel mediated mechanisms of neurotransmission, or GABAergic receptor mediated intracellular mechanism of action that is preeminently responsible
15 for drug response. By embarking on the previously described gene pathway approach, it is technically feasible to determine the relevant genes within such a targeted drug development program for spasticity.

A sample of therapies approved or in development for preventing or treating the progression of symptoms of spasticity currently known in the art is shown in
20 Table 36. In this table, the candidate therapeutics were sorted and listed by mechanism of action. Further, the product name, the pharmacologic mechanism of action, chemical name (if specified), and the indication is listed as well.

Description of Mechanism of Action Hypotheses for Future Drug Development for Spasticity

25 Although the exact mechanism of neurodegeneration-induced spasticity is unknown, the pathophysiology centers on the inadequate release of the inhibitory neurotransmitter, GABA within the spinal cord. Cerebral damage or localized damage within the spinal cord can influence the descending neurons that normally release GABA. However, the afferent input to the spinal cord from the muscle
30 spindles is unaffected causing a relative increase of excitatory neurotransmitters, particularly glutamate. The consequence is excessive stimulation of the alpha motor neurons resulting in spasticity. Spasticity arising from cerebral damage may only affect certain modulatory inhibitory signals resulting in a variability of spasticity within each and among patients. Since all muscle groups may not be affected
35 equally, management may be complicated.

Spastic paresis or spastic dystonia appear to arise from an imbalance of inhibition and excitation occurring at the level of the motor neuron. The most basic

component is the abnormal intraspinal response to sensory input. Since modulation of the local spinal cord activity (peripheral segmental reflex arcs and the anterior horn cells) occurs via the descending pathways, loss of the GABA interneurons can affect the balance of excitation/inhibition and leads to hyperexcitable cells that result in an increase in activity of by the extrafusal muscle fibers.

Further, there may be genes within pathways that are either involved in metabolism of neurotransmitters or are involved in metabolism of various drugs or compounds. In Tables 2, 13, and 19, there are listings of candidate genes and specific single nucleotide polymorphisms that may be critical for the identification and stratification of a patient population diagnosed with spasticity based upon genotype. Current pathways that may have involvement in the therapeutic benefit of epilepsy include glutaminergic, adrenergic, cholinergic, GABAergic, calcium channel, mitochondrial maintenance, adhesion, and myelination gene pathways that are listed in Tables 2, 13, and 19. One skilled in the art would be able to identify these pathway specific gene or genes that may be involved in the manifestation of spasticity, are likely candidate targets for novel therapeutic approaches, or are involved in mediating patient population differences in drug response to therapies for spasticity.

G. Ischemic Cerebrovascular Disease

Description of Stroke

Ischemic cerebrovascular disease is a result of an imbalance of the oxygen supply and the oxygen demand of brain tissue. Stroke is a series of clinical manifestations of reduction of blood supply to the cerebrovascular bed. The signs and symptoms may be complex and depend on the location and extent of the infarct. Ischemic cerebrovascular disease is divided into thrombotic and hemorrhagic stroke.

Thrombotic Strokes

Strokes are the result of reduced blood flow supplied by one or more of the major cerebral arteries. Blockage or reduction of blood volume to these main arteries manifests as identifiable neurological symptoms. For example, occlusion of the middle cerebral artery results in contralateral hemiparesis, expressive aphasia, anosognosia and spatial disorientation, contralateral inferior quadrantanopsia, contralateral hemiparesis, sensory loss, contralateral homonymous hemianopsia, or superior quadrantanopsia. Blockage or reduction of the inner carotid artery, anterior cerebral artery, vertebral or basilar arteries, or the posterior artery can result in similarly clinically distinct neurological symptoms.

Transient ischemic attacks (TIA) are similar to a thrombotic stroke in that neurological deficit lasts for a brief period and is generally treated with potent platelet aggregation inhibitors.

Thrombotic strokes are the result of focal blockage of one or more of the cerebral arteries or branches resulting in neurological signs and symptoms lasting greater than one hour. Artherosclerotic plaques in extracranial or intracranial arteries cause approximately two thirds of thrombotic strokes. Embolization, stenosis, or occlusion of one or more of the cerebral arteries or branches may cause thrombotic strokes. Emboli can be of cardiac origin (e.g. mural thrombi, valvular heart disease, arrhythmias (atrial fibrillation), cardiac myxoma, and paradoxical emboli (venous origin). Focal ischemia may also be the result of inflammation and necrosis of extracranial or intracranial blood vessels, i.e. vasculitides (e.g. primary cerebral arteritis, giant cell vasculitis, infectious vasculitis) or the result of hematologic abnormalities (hemoglobinopathy, hyperviscosity syndrome, hypercoagulable states, protein C or S deficiency, the presence of antiphospholipid antibodies). Strokes may be drug related, for example illicit drugs (cocaine, "crack", amphetamines, lysergic acid, phencyclidine, methylphenidate, sympathomimetics, heroin, and pentazocine), ethanol, and oral contraceptives. Lastly there are other diseases that may predispose an individual to a stroke, for example fibromuscular dysplasia, arterial dissection, homocystinuria, migraine, subarachnoid hemorrhage, vasospasm, emboli of other origin (fat, bone, and air), and moyamoya.

Hemorrhagic Strokes

Approximately 20% of all strokes are the result of intracranial hemorrhage. Approximately half of these cases are into the subarachnoid space and the other half directly in the cerebral tissue. The acute rise in intracerebral pressure generally results in loss of consciousness and many die of cerebral herniation. Similar to thrombotic strokes, hemorrhagic strokes can be considered diffuse or focal, depending on the extent of the vessel disruption. Causes of spontaneous intracranial hemorrhage include arterial aneurysms (berry aneurysms, fusiform aneurysm, mycotic aneurysm, and aneurysm with vasculitis), cerebrovascular malformations, hypertensive-atherosclerotic hemorrhage, hemorrhage into a brain tumor, systemic bleeding diatheses, hemorrhage with vasculopathies, hemorrhage with intracranial venous infarction. Subarachnoid hemorrhage is caused by rupture of surface arteries (aneurysms, vascular formations, head trauma) with blood limited to the cerebrospinal fluid space between the pial and the arachnoid membranes.

Current Therapies for Stroke

If a hemorrhagic stroke is clear on the CCT, gradual reduction of systemic BP is achieved by standard vascular dilatation medications. Angiography can be useful to identify the source of the hemorrhage. Surgical management of the hemorrhage may be required.

If an ischemic stroke is identified and focal neurological impairments subside over time, a transient ischemic attack (TIA) is suspected. TIA has a high rate of recurrent stroke within a short time frame. Platelet aggregation inhibition is standard therapy; aspirin or ticlopidine. Ticlopidine is associated with neutropenia and agranulocytosis which may be life threatening. Because of these severe side effects, Ticlopidine is reserved for patients who are intolerant to aspirin therapy.

If angiographic review a clearly defined clot is detected, TIA may be surgically treated with endarterectomy.

For the treatment of thrombotic or embolic strokes, each case is independently assessed for surgical management or anticoagulant therapy. The success of thrombotic therapy, e.g. tissue plasminogen activator (tPA), streptokinase, urokinase, relies on timely reperfusion. The therapeutic window for tPA has been shown to be within three hours of onset of symptoms. Hypothermia has been shown to decrease mortality and improve outcomes. Hyperthermia has been shown to worsen both mortality rates and outcomes.

Significant neurologic improvement has been shown to occur within the first three months after stroke symptoms. A clear focus on intensive rehabilitation during this critical time frame has been shown to enhance the eventual outcome for survivors of stroke.

Limitations of Current Therapies for Stroke

The single most limiting factor of stroke therapy is the rapid identification of stroke symptoms and urgency of intervention within a short time.

Limitations of Stroke Therapy Due to Low Efficacy and Deleterious Side Effects

Guidelines for the use of tPA in acute ischemic stroke call for the administration of the thrombolytic agents within the first three hours from the onset of symptoms. After three hours four probable deleterious effects have been proven in animal studies and are as follows: 1) cerebral and extracerebral hemorrhage, 2) reperfusion injury, 3) fragmentation of clots, and 4) reocclusion of reperfused vessels.

In both animal models and in humans, reperfusion therapy must be administered within three hours of symptom onset. After three hours deleterious reperfusion injury may occur. Mortality at three months was 17% in the tPA group and 21% in the placebo group ($p=0.30$). Tissue plasminogen activator (tPA), streptokinase, heparin, and urokinase have specific restrictions: tPA has a 6% rate of cerebral hemorrhage; streptokinase is generally not used for thrombotic strokes because of serious side effects and limited quantifiable efficacy, urokinase is generally delivered near the site of the clot or obstruction. Factors influencing the best medical treatment of ischemic stroke must weigh the benefits and limitations of each of these therapies.

Impact of Genotyping on Drug Development for Stroke

As described above, there is evidence to suggest that there are efficacy and safety differences to drug therapy in the stroke patient population. Although not all of these responses may be attributable to genotypic differences, it is expected that if stratification based upon genotype were performed, a reasonable correlation between drug response and genotype may become obvious. As described below, there are gene pathways that are involved with current drug therapy and those that may be potentially involved in the future. As described in the Detailed Description, methods for the identification of candidate genes and gene pathways, stratification, clinical trial design, and implementation of genotyping for appropriate medical management of a given disease is easily translated for stroke patients. As described below in section V. below there are likely gene pathways as are those that are outlined in the gene pathway Table 2 and matrix Table 7.

A sample of therapies approved or in development for preventing or treating the progression of symptoms of stroke currently known in the art is shown in Table 37. In this table, the candidate therapeutics were sorted and listed by mechanism of action. Further, the product name, the pharmacologic mechanism of action, chemical name (if specified), and the indication is listed as well.

Mechanism of Action Hypotheses for Novel Therapies for Stroke: Utility of Genotyping

There are two categories of genotyping that provided insight on the selection of candidate genes for polymorphic genotypic studies of drug response. One set of likely candidates come from disease etiology or linkage studies. These data may provide input on the genetic etiology or aberrant mechanisms of strokes. Another set are those genes involved in the biochemical or molecular mechanisms of drugs, agents, or candidate therapeutic interventions.

Genes Involved in the Etiology of Stroke

Studies have demonstrated that there is a genetic component to thrombotic stroke. These genetic factors may predispose by an individual to thrombotic stroke by inheriting one or more of the following 1) low threshold for aberrant formation of atherosclerotic plaques in intracranial blood vessels; 2) traits that underlie certain specific etiology of stroke; and 3) a disease, disorder, or pathophysiologic process of the CNS in which there are associated molecular or structural disturbances that predispose individuals to strokes. These genetic influences mediating stroke may be candidates for genotyping assays and directly linked to pharmacogenomic programs.

Genes Involved in the Mechanism of Drug Action

There are also the biochemical, or molecular mechanisms of drug or candidate therapeutic action that may affect drug action. As described above there is an urgent need for the discovery and development of therapeutic alternatives for the medical management of strokes in which therapy commences beyond the therapeutic windows of thrombolytics.

Recent research and development programs have included the following pathways: 1) glutamate neurotransmitter pathway has been implicated in aberrant excitatory neurotransmission; 2) inflammation is a mechanism that may lead to profound neural cell loss, 3) carnosine pathway, 4) cell adhesion pathways, 5) oxidative stress pathways, 6) growth factor mediated differentiation and rescue of ischemic tissue, and protein maturation and degradation.

Ischemic Penumbra, Site of Infarct-Tissue at Risk

Ischemic penumbra is the tissue immediately adjacent to the infarct zone that is viable and morphologically intact but functionally impaired due to the restricted blood flow. Once the blood flow decreases to a certain threshold, this penumbra tissue can be classified as "misery-perfused" because oxygen consumption is preserved and increased oxygen extraction occurs. Ischemic penumbra is, thus, a dynamic process of impaired perfusion and unstable energy metabolism. Since necrosis naturally follows the continued oxygen deprivation, it has been reported that final cerebral infarct size is infarct zone plus the unrecoverable penumbra.

Functional imaging of the cerebral infarct can detect the penumbra tissue, and in some reports the penumbra tissue can be identified up to 48 hours. There is controversy whether the penumbra tissue can be rescued and what is the appropriate time from symptom onset to rescue by reperfusion. Rescue and time to rescue by reperfusion is dependent on the extent of occlusion and severity of metabolic disturbances. Based upon the hypothesis that early, immediate reperfusion can

restore blood flow, the therapeutic window for successful intervention to restore the metabolic alterations has been postulated and proven to be within the first three hours from symptom onset. Other therapies include restoration of the cytokine, neurotransmitter, and Ca^{+2} concentrations within the infarct zone (see therapy for stroke below).

Since the therapeutic window for victims of stroke is narrow and the debilitating effects of an ischemic stroke can be both costly and severely impact health-related quality of life, there is demand for candidate therapeutic interventions that can halt, retard, prevent neural destruction. Furthermore, there is a demand to develop further candidate therapeutic interventions that can assist in the rehabilitation and ultimately improve the health-related quality of life indices.

Inflammation and Immune Disease, Disorders, or Dysfunctions

Exemplary diseases characterized by abnormal inflammatory or immunologic responses (also referred to herein as inflammatory or immune diseases or disorders) are described below. These diseases are suitable for application of the methods described in this invention for identification of variances in a gene or genes involved in therapeutic response, e.g. efficacy, tolerability or toxicity.

A. Arthritis

Description of Arthritis

Arthritis comprises a variety of diseases characterized by pain, swelling, and limited movement in joints and connective tissues. Arthritis is usually chronic and there are three prevalent forms of the disease: rheumatoid arthritis (RA), osteoarthritis (OA), and fibromyalgia. In RA, the synovial joint lining becomes inflamed as a result of hyperactive immune response. There are an estimated 2.1 million Americans with RA; two thirds are women. In OA, the cartilage that covers the ends of the bones within joints deteriorates, causing pain and loss of movement as bone begins to rub against bone. There are an estimated 20.7 million Americans with OA, the majority being over the age of 45. In fibromyalgia, widespread pain affects muscles, attachments of muscles to bone, and the connective tissues, i.e., the ligaments and tendons. There are an estimated 3.7 million individuals diagnosed with fibromyalgia syndrome. Other serious and common forms of arthritis or related disorders include the following: gout, systemic lupus erythematosus, scleroderma, ankylosing spondylitis, and juvenile arthritis.

Rheumatoid arthritis involves the disarthroidal joints and can affect a variety of other organs. The clinical hallmarks of RA include: morning stiffness; swelling of three or more joints; swelling of hand joints (proximal interphalangeal, metacarpophalangeal, or wrist); symmetric swelling; subcutaneous nodules; serum

rheumatoid factor; and erosions and or periarticular osteopenia, in hand or wrist joints, often observed on radiograph.

Osteoarthritis is a degenerative process in joint tissues that may occur in response to aging, genetic, and environmental factors. It is characterized by progressive degeneration of cartilage, bone remodeling, and overgrowth of bone. The clinical hallmarks of OA include: deep aching pain in the afflicted joints (hands, knees spine, and hips), morning stiffness of short duration, variable joint thickening and effusion. Pathologically OA is characterized by breakdown of cartilage. Destruction of joint cartilage involves direct physical injury, enzymatic degradation as a result of the injury to chondrocytes, and subchondral bone stiffening as a result of the bone remodeling.

Current Therapies for Arthritis

Agents used to treat RA fall into one of the following four categories: analgesics (NSAIDs, salicylates), disease modifying antirheumatic agents (gold compounds, cytotoxic), hormones (glucocorticoids), and skin and mucosal membrane preparations. Therapies for the treatment of OA focus on decreasing pain (analgesics) and physical therapies to increase joint mobility.

Analgesics: Typically, pain associated with arthritis can be controlled with NSAIDs including but not excluded to, salicylates, para-aminophenol derivatives, indole and indene derivatives, heteroaryl acetic acids, arylpropionic acids, anthranilic acids, enolic acids, or alkanones. Antiinflammatory agents such as cyclooxygenase inhibitors, lipoxxygenase inhibitors, and others can be used to block the inflammation physiological pathway which mediate pain and the progression of the disease. However, because these drugs are limited in their efficacy in advanced or more severe stages of arthritis, these agents are add-on therapies.

NSAIDs derive their principle mechanism of action by the inhibition of prostaglandin and leukotriene synthesis. These compounds inhibit key enzymes in the biosynthetic pathway, i.e. cyclooxygenase. There are drugs that selectively inhibit isoforms of cyclooxygenase 1 and 2 (COX-1, COX-2) which enhances patient tolerance due to the prevalence of COX-2 induction occurs in inflammation mediated by cytokines and others.

Further, pyrimidine synthesis inhibitors can be used as an antiinflammatory agent in arthritis, e.g. leflunomide.

Disease-Modifying Antirheumatic Drugs or agents: Agents involved in the modification of clinical disease manifestation, reduction in inflammation, or slow the progression of the disease are referred to as disease-modifying antirheumatic drugs (DMARDs) and include gold salts (aurothioglucose, aurothiomalate,

auranofin), hypotensives (angiotension converting enzyme inhibitors), anaprox, immunosuppressives (azathioprine, cyclosporine), agents to treat metallic poison (penicillamine), depen, naprosen, immuran, antimalarials (chloroquine, hydroxychloroquine), alkylating agents (cyclophosphamide), absorbable
5 sulfonamides (sulfasalazine), irritants and counter-irritants (capsaicin), antimicrobial agents (tetracyclines), and antimetabolites (methotrexate).

Hormones and Growth Factors: Agents acting at hormone receptors or growth factor receptors include steroids (glucocorticoids), adrenocorticotrophic hormone (corticotropin), and tumor necrosis factor inhibitors (soluble TNF receptors
10 (enbrel) and TNF monoclonal antibody (remicade). Since the autoimmunity component of the disease is driven primarily by activated T-cells, which give rise to cytokines IL-1 and TNF at the rheumatoid synovium. These agents are known to interfere with the actions of these cytokines.

Corticosteroids affect the inflammation within the joints by decreasing
15 growth and development of mast cells, inducing apoptosis, suppressing lymphocyte generation of IL-5 and other cytokines, inhibiting some mediator release, inhibiting cytokine production, inhibiting the transcription of cytokines (for example IL-8, TNF- α , prototypic antiviral chemokine (regulated-on-activation normal T-expressed and secreted, RANTES), and GM-CSF), and inhibiting nitric oxide synthesis.

20 Skin and mucosal membrane preparations: irritants and counter-irritants can be used to treat arthritic joints and include, but not limited to, Capaicin

Chlorambucil, cyclosporine, cyclophosphamide are agents that are available for use in the treatment of refractory RA or with severe extraarticular complications such as vasculitits, corneal perforation or other severe systemic maladies associated
25 with RA.

Low Efficacy Limitations of Therapies for Arthritis

The therapies discussed above are limited to the slowing or retarding the progression of arthritis. As degeneration of the joints progresses, and irreversible
30 damage occurs, the options become limited. Thus, therapies for arthritis are aimed at reduction of manifestation of symptoms by controlling the clinical manifestations of inflammation.

The reduction of clinical symptoms of arthritis following DMARDs therapy is only evident after several weeks to months after therapy. The slow clinical
35 relevance of these therapies limits the clinician to determine optimal therapy for individuals with arthritis, and provides a risk for selection of optimal therapy for any given stage of the disease.

Toxicity or Undesired Side Effects as Therapeutic Limitations of Arthritis

There are toxicities and undesired side effects associated with the above current therapies for arthritis that require monitoring. Drugs used to treat arthritis may cause death, disability, disease, and place an unborn child at risk. The undesired side effects or toxicities are listed for each drug category as described above.

Analgesics associated side effects include dyspepsia, gastric or small bowel bleeding, ulceration, renal insufficiency, confusion, rash, headache, hepatic toxicity. NSAIDs also reversibly inhibit platelet aggregation and prolong bleeding time.

Antirheumatic agents (DMARDs) associated side effects include antimalarials: retinal or macular damage; sulfonamides: hematologic toxicities (leukopenia, thrombocytopenia, hemolysis in patients with glucose 6-phosphate dehydrogenase (G6PD) deficiency); antimetabolites: hepatic compromise including hepatic fibrosis, ascites, esophageal varices, cirrhosis, pneumonitis, myelosuppression; immunosuppressives: myelosuppression, (cyclosporine: renal insufficiency anemia, hypertension); agents to treat metallic poison: rash, stomatitis, dysgeusia or metallic taste, myelosuppression (thrombocytopenia), proteinuria, nephrotic syndrome or renal failure, and induction of autoimmune syndromes (systemic lupus erythematosus, myasthenia gravis, polymyositis, Goodpasture's syndrome), gold preparations: hematologic, renal, pulmonary, and proteinuria; chlorambucil: myelosuppression, myeloproliferative disorders, malignancy, hemorrhagic cystitis.

Soluble TNF receptors agents have been shown to induce sepsis and predispose patients to serious infections. Further this product was associated with site of injection reactions, infections, and headache.

Glucocorticoid associated side effects include increased appetite, weight gain, fluid retention, acne, ecchymosis, development of cushoid facies, hypertension, hyperkalemia, diabetes, hyperglycemia, hyperosmolar state, hyperlipidemia, hepatic steatosis, atherosclerosis, myopathy, aseptic necrosis, osteoporosis, ulcers, pancreatitis, psuedotumor cerebri, psychosis, glaucoma, cataract formation, vascular necrosis, increased susceptibility to infection, impairment of the hypothalamus-pituitary axis, decreased thyroid hormone serum binding proteins, and impaired wound healing.

Since the majority of RA patients are women in their reproductive years, the level and extent the agents used to treat RA affects or has a potential to affect the mother during pregnancy, cross the placenta, affect the developing fetus, or be excreted in breast milk during lactation are important issues facing the skilled practitioner. Clinical medical therapeutic decisions must weigh the use of all of the

above current therapies for RA against known capacity of these agents to affect both the mother and the child.

5 Description of Mechanism of Action Hypotheses for Future Drug Development for Arthritis

Rheumatoid arthritis has been thought to be the result of host genetic factors, immunoregulatory abnormalities and autoimmunity, and triggering or persistent microbial infection.

10 Host genetic factors: the HLA-DR4 antigen (HLA, human leukocyte antigen) is significantly increased in RA patients. Recent studies have determined that a subtype of the HLA-DR4 share similar epitope among several MHC class II molecules and predispose to RA.

15 Autoimmune component: in over 80% of RA patients autoantibodies to the Fc portion of IgG (rheumatoid factors, RF) are present and can be used to determine diagnosis. The higher the titer of RFs the more severe joint disease and extrarticular manifestations.

Related to the autoimmune component of the disease, ICAM-1 inhibitors, or other agents to reduce adhesion have been developed.

20 Microbial Infections: of all the examined pathogens, only the Epstein-Barr virus (EBV) has remained unproven as a cause of RA. EBV has been shown to share a similar epitope as the HLA-DR4 epitopes, but EBV is ubiquitous and has yet to be a proven cause of RA.

25 A gene, genes, or gene pathway involved in the etiology of arthritis or associated disorders or potential sites for targeted drug therapy of arthritis are depicted in Table 9 with the specific gene list in Table 4. Current candidate therapeutic interventions in development for the treatment of arthritis are listed in Table 38.

30 B. Chronic Obstructive Pulmonary Disease

Description of Chronic Obstructive Pulmonary Disease

Chronic obstructive pulmonary disease (COPD) is an imperfect term that refers to four pulmonary disorders including simple chronic bronchitis, asthmatic bronchitis, chronic obstructive bronchitis, and emphysema. A common characteristic of the disease is airway obstruction. Airways obstruction denotes the slowing of forced expiration. A decrease in the forced expiratory volume in 1 second (FEV1) to forced vital capacity (FVC) indicates that airflow is impaired. Forced expiration is determined primarily by intrinsic resistance of the airways, compressibility of the airways, and lung elastic recoil. Reduced maximal expiratory

flow results from high airway resistance, reduced lung recoil, or excessive airways collapsibility. The overall cost of these illnesses to society is enormous due to the extent of the number of individuals afflicted with COPD, approximately 15 million Americans, and that COPD is currently the fourth-leading cause of mortality. The high morbidity and mortality rates associated with COPD are linked to the failure to identify at-risk patients and intervene. The lungs have large reserves of pulmonary function and the slow progressive nature of the disease can often delay the clinical diagnosis and therapeutic intervention.

Simple chronic bronchitis is a syndrome predominantly characterized by chronic productive cough and is usually the result of low-grade exposure to bronchial irritants. This syndrome is associated with enhanced mucous secretion, reduced ciliary activity, and impaired resistance to bronchial infection. Bronchitis patients range from those who experience sporadic cough producing mucous to those with a severe, disabling condition manifested by one or more of the following: increased resistance to airflow, hypoxia, hypercapnia, and irreversible narrowing of the small airways, i.e. bronchioles and bronchi (2 mm or less in diameter).

Repeated exposure to bronchiole irritants in individuals with hyperactive or sensitive airways can lead to bronchospasm, i.e. bronchial smooth muscle constriction, that is frequently accompanied by excess mucous production and edema of the bronchial walls. Episodic bronchospasm in individuals with chronic bronchitis is termed asthmatic bronchitis and is applied to those individuals with chronic airway constriction, chronic productive cough, and episodic bronchospasm.

Emphysema is characterized by abnormal, excessive, permanent enlargement of airway spaces distal to the terminal bronchioles, and is accompanied by destruction of their walls and may or may not be associated with fibrotic tissue. These changes result in a reduction of elastic recoil permitting excessive airway collapse upon expiration and leads to irreversible airway flow obstruction. Emphysema is strongly related to and correlated to inhalation of tobacco smoke, i.e. cigarette or cigar smoking.

In emphysema there is a loss of elastic recoil leading to pulmonary hyperinflation. The hyperinflation reaches a limit when the diaphragm is pushed flat and no longer functions effectively. The chest wall is expanded to the point that it pushes inward rather than exerting its normal outward force. These anatomical changes alter inspiration to the point that exertion is nearly impossible.

A deficiency in alpha 1- antitrypsin can predispose individuals to signs and symptoms of COPD. In these individuals there is a marked alveolar wall destruction with a non-uniform pattern of air space enlargement. In these patients there may be excessive formation of thick mucous and is often accompanied by persistent cough.

Complications of COPD include hypoxemia, cor pulmonale, hypercapnia, and dyspnea. Sustained chronic hypoxemia is a condition that leads to pulmonary vasoconstriction that with time becomes irreversible and leads to cor pulmonale.

Current therapies for COPD

The current therapies is use for the treatment of subjects with COPD are aimed at reducing the airway obstruction that is reversible, controlling the persistent cough and sputum production, reducing or eliminate airway infections, increasing exercise tolerance to the maximum allowable at the individual's level of physiological deficit, controlling the remedial disease complications, i.e. cardiovascular dysfunction and arterial hypoxemia, and relief of the anxiety and depression or other psychiatric symptoms that accompany patients attempts to cope with the debilitating clinical manifestations. Lastly, all treatment regimens include education and supportive therapy to encourage subjects with COPD to cease behaviors that may exacerbate symptoms such as inhalation of pulmonary irritants, i.e. smoking and others, and substance abuse, i.e. narcotics and sedatives.

Bronchodilators

Bronchodilators can be inhaled, or by oral, subcutaneous, or intravenous routes.

Beta-adrenergic agonists or other sympathomimetic agents are used to produce rapid acute bronchodilation.

Anticholinergics agents are used to produce sustained bronchodilation. Nebulized atropine has been supplanted with the advent of a quaternary ammonium salt, ipratropium bromide, which undergoes minimal systemic absorption and thus has limited anticholinergic toxicity. Ipratropium has been shown to be effective in patients that have not responded to β -adrenergic agonists and can reduce sputum volume without altering viscosity.

Anticholinergics and beta-adrenergic agonist combinations have been used with some success. Such combinations reduce the need to administer high doses, due to additive effects, and therefore reduce the likelihood for adverse effects or toxic side effects.

Theophylline is a methylxanthine bronchodilator. Theophylline improves airway flow, decreases dyspnea, reduces pulmonary arterial pressure, increases arterial oxygen tension, improves diaphragmatic strength and endurance, increases right ventricular function (pulmonary vasodilator and cardiac inotropic effects), and may produce antiinflammatory effects.

Expectorants

Expectorants can be used to increase the secretion clearance in patients with COPD. Although this therapy has not been demonstrated to render clinical benefit, it is as add on therapy that enables the patient to experience an enhanced productive cough.

5 Anti-Inflammatory agents

Prolonged use of corticosteroids have been used to retard the rate of decline in FEV1 in COPD subjects. However, it has been determined that systemic corticosteroids are beneficial for acute exacerbations of COPD but are not used for long-term treatment and have not been proven to retard the progression of the
10 disease. Corticosteroids affect the decline of FEV1 in the airways by decreasing growth and development of mast cells, inducing apoptosis, suppressing lymphocyte generation of IL-5 and other cytokines, inhibiting some mediator release, inhibiting cytokine production, inhibiting the transcription of cytokines (for example IL-8, TNF- α , prototypic antiviral chemokine (regulated-on-activation normal T-expressed and secreted, RANTES), and GM-CSF), and inhibiting nitric oxide synthesis.
15

Antiproteases and antioxidants

Alpha1-protease inhibitor deficiency as a cause of early development of emphysema has increased the awareness of the role of protease-antiprotease and oxidant-antioxidant imbalances in COPD. Intravenous delivery of alpha 1-protease
20 inhibitor can provide the appropriate levels in those individuals with a genetic deficiency and those whose deficiency is acquired.

Mucolytics and secretion clearance agents can be used to assist in the removal of secretions during productive cough. These agents can thin secretions in patients with chronic bronchitis.

25 Supplemental oxygen therapy is used to treat the deleterious effects of sustained chronic hypoxemia and hypercapnia. Correction of this condition is one of the treatments shown to have a positive effect on the survival rate in patients with COPD.

30 Treatment of cases of cor pulmonale includes the use of diuretics and positive inotropic agents such as digitalis. Careful monitoring is required in these patients due to a development of marked right ventricular hypertrophy.

Dyspnea may be severely disabling despite aggressive therapy. Judicious use of opiates to control dyspnea and increase exercise tolerance have been proven to be beneficial. Unfortunately, opiates can have a respiratory depressant effect and
35 care must be taken to deliver the appropriate therapeutic dose.

Many patients with COPD find themselves anxious or depressed or both. Appropriate use of psychoactive agents can be used to control the signs and symptoms of anxiety and depression.

Surgical procedures can be performed to attempt to restore pulmonary capacity and function. Lung volume reduction surgery is useful to remove a portion of emphysematous lung tissue so that the diaphragm can return to its normal dome shape and the chest wall can reassume its normal configuration, mechanics, and physiology. Bullectomy is a procedure in which large bullae and surrounding lung tissue are removed. This allows for the remaining tissue to expand and once again function normally. Another procedure is lung transplantation. This expensive and aggressive approach is usually reserved for younger patients, particularly those who are alpha 1-antitrypsin deficient.

Limitations of Current Therapies for COPD

The most common limitations for the use of bronchodilators is the mistaken use of inhalants and inadequate patient education.

Beta adrenergic therapy is limited by three factors: 1) the density of β_2 receptors in the airways decreases with age, 2) despite the selectivity of the β_2 receptor agonists, there is cross reactivity to β_1 receptors and may affect the myocardium and other peripheral tissues, and 3) there is β -adrenergic receptor desensitization. Most of the recommended doses of beta adrenergic agonists provide less than maximal bronchodilation. Beta-adrenergic agonists can cause tremor, reflex tachycardia, tachyphylaxis, cardiomyopathy, and other cardiac toxic effects. Tachycardia is particularly problematic in the elderly or for those individuals who are at cardiac risk. Further, β -adrenergic agonists have been shown to cause hyperkalemia. The majority of patients with COPD are current or former smokers, all of whom are may have coexisting coronary artery disease, thus in the compendium of therapies it is desirable to have alternatives to β -adrenergic agonists.

Anticholinergics as bronchodilators have been associated with systemic side effects. In particular, systemic anticholinergic side effects include bradycardia (if pronounced, includes compensatory tachycardia), dry mouth, inhibition of sweating, dilatation of the pupils, and visual blurring. Ipratropium has a slow onset of action and a longer duration of action than β -adrenergic agonists which can be deleterious for acute bronchodilation because patients continue to administer the drug without effect and overdose.

Theophylline continues to be a controversial treatment due to misconceptions of its role as a bronchodilator, drug delivery problems, and conflicting results of comparative studies during acute exacerbations. Further, theophylline has a limited therapeutic window, i.e. the dose required to achieve bronchodilation is close to the dose associated with undesirable or adverse side effects including convulsions,

cardiac arrhythmias, tachycardia, vasodilation, and diuresis. Further complicating therapy with theophylline is the intra-patient variability in efficacious response.

Long-term use of corticosteroids can be useful for patients in which continued symptoms or severe airflow limitations exist despite therapy with other agents. Only 20-30% of these patients experience therapeutic benefit for long-term use and indiscriminate use often leads to adverse effects without benefits.

Unfortunately there have not been identified predictors of responders or nonresponders to long term steroid use in patients with COPD. Therefore, only those patients that attempt long-term steroid use and have documented clinical improvement should continue steroid therapy. Unfortunately, those patients in which long-term steroid use results in no benefit are subjected to potential adverse effects or toxicities. Glucocorticoid associated side effects include increased appetite, weight gain, fluid retention, acne, ecchymosis, development of cushoid facies, hypertension, hyperkalemia, diabetes, hyperglycemia, hyperosmolar state, hyperlipidemia, hepatic steatosis, atherosclerosis, myopathy, aseptic necrosis, osteoporosis, ulcers, pancreatitis, pseudotumor cerebri, psychosis, glaucoma, cataract formation, vascular necrosis, increased susceptibility to infection, impairment of the hypothalamus-pituitary axis, decreased thyroid hormone serum binding proteins, and impaired wound healing.

Mucolytic and secretion clearance agents have been shown to improve thinning secretions however, there is little evidence to suggest that these agents render clinical improvement. Further cough suppressants may impair secretion clearance and possibly increase the risk of pulmonary infection.

Description of Mechanism of Action Hypotheses for Future Drug Development of Candidate Therapeutic Interventions of COPD

Since the predominant category of patients with COPD were or are current smokers smoking cessation programs and agents used to help patients quit smoking will be a valuable addition to therapeutic regimens. Nicotine replacement therapies such as nicotine patches (transdermal), gum, and transnasal formulations as well as bupropion (an antidepressant or other in this category) should be considered.

Other therapies to be considered are novel bronchodilators for inhalation therapy without the use of chlorofluorohydrocarbons (CFCs), next generation anticholinergic therapies, alpha 1 antiproteinase augmentation therapies, and refinement of surgical procedures.

A gene, genes, or gene pathway involved in the etiology of COPD or associated disorders or potential sites for targeted drug therapy of COPD are depicted in Table 9 with the specific gene list in Table 4. Current candidate

therapeutic interventions in development for the treatment of COPD are listed in Table 39.

C. Autoimmune Disease

Description of Autoimmune disease

An immune response to “self” antigens, or autoimmunity, can vary from minimal to severe depending on the extent of the loss of self tolerance and to the localization of the antigens. There is then a distinction between autoimmune response which may or may not be pathologic and autoimmune disease which does lead to pathologic conditions. In autoimmune disease there is a combination of the following types of evidence, 1) identification of the target antigens, 2) identification and isolation of self-reactive autoantibodies or self-reactive lymphocytes, 3) identification of clinical evidence, i.e. familial hereditary data, lymphocyte infiltration, MHC association and clinical symptomatic improvement with immunosuppressive agents. Initiation of autoimmune disease is thought to require one or more of the following: genetic predisposition to loss of tolerance, environmental factors that stimulate aberrant immune response, or loss or dysfunction of cellular or organ physiological processes leading to pathological immune response. Since many autoreactive clones of T and B cells exist and are normally regulated by homeostatic mechanisms, loss or breakdown of this system of checks and balances can lead to activation or enhancement of these autoreactive clones and ultimately lead to autoimmune disease.

There are a few autoimmune disease indications whereby inflammation and immune response gene pathways should be considered in the stratification or therapeutic choice of patient groups based upon genotype. There are multiple examples of autoimmune diseases or diseases that have an autoimmune component including: amyotrophic lateral sclerosis, anti-phospholipid syndrome, aplastic anemia, autoimmune hemolytic anemia, diabetes mellitus type 1, Guillan-Barre syndrome, idiopathic thrombocytopenic purpura, Grave’s disease, myasthenia gravis, polymyositis, rheumatoid arthritis, Hashimoto’s thyroiditis, uveitis, Wegener granulomatosis, periarteritis nodosa, ocular pemphigoid, pemphigus vulgaris, psoriasis, Goodpasture’s syndrome, Churg-Strauss vasculitis, poly-dermatomyositis, Cogan syndrome- autoimmune inner ear disease, hemolytic uremic syndrome, idiopathic glomerulonephritis, inflammatory bowel disease, Crohn’s disease, microscopic polyarteritis, and multifocal motorneuron neuropathy. Here we discuss four specific diseases that represent larger patient populations and are representative of diseases in which therapy can be aimed at suppressing the hyperactivity of the

immune system. These include multiple sclerosis, systemic lupus erythmatosus, scleroderma, diabetes mellitus type I, sarcoidosis, and nephritis.

Multiple Sclerosis

Multiple sclerosis (MS) is a disorder of multifocal sites of myelin sheath
5 destruction, perivascular-lymphocytic cuffing and variable degree of
oligodendroglial loss. In profound cases, there is gliosis, axonal transection, and
neuronal and axonal loss. There are an estimated 300,000 Americans diagnosed
with MS. The estimated cost of MS is \$5 billion dollars.

Clinically, MS begins with a relapsing illness with episodes of neurological
10 dysfunction lasting several weeks, followed by substantial or complete
improvement. This is identified as the relapsing-remitting stage of the disease found
to be predominantly in females (1.6:1). There are some patients that remain in this
stage of the disease for decades; others may rapidly progress to the next stage. As
time progresses, and repeated relapses occur, recovery becomes less and less
15 complete or as substantial. In these cases, a gradual relapse independent clinical
progression develops and is termed secondary progressive MS. Further, the
nonrelapsing-nonremitting form is characterized by a gradual progression and steady
worsening of neurological function without any recovery or improvement. A steady
but gradual neurological decline and predominately identified in males characterizes
20 the primary progressive form of MS. Clarity in understanding the significance of
these varying disease patterns and diagnosis is dependent on quality neurological
examination overtime.

Systemic Lupus Erythmatosus

Systemic lupus erythmatosus (SLE) is a disease characterized by
25 inflammation in many different organ systems associated with the production of
antibodies to reactive to nuclear, cytoplasmic, and cell membrane antigens. Clinical
manifestations of the disease include reddish rash on the cheeks, fatigue, anemia,
rashes, sun sensitivity, alopecia, arthritis, pericarditis, pleurisy, vasculitis, nephritis,
and central nervous system disease. The immune hypereactivity appears to derive
30 from immune hypereactivity and loss of self-tolerance. In these patients antibodies
are produced against several nuclear components, notably antinuclear antibodies to
native double stranded DNA, single stranded DNA, or nucleohistones.

Scleroderma

Scleroderma is a chronic disease marked by increases of fibrotic tissue
35 involving the circulatory system, connective tissue (in particular the skin), visceral
organs, and the immune system. There are approximately 500-700,000 Americans
diagnosed with scleroderma. There are two types of scleroderma, localized and
systemic. In localized scleroderma (linear and morphea) the disorder of the

connective tissue is limited to the skin, the tissues just beneath the skin, and muscle. Internal organs are not affected. In systemic scleroderma (sclerosis) vascular, digestive, pulmonary, renal, muscle and joints may be affected. Raynaud's syndrome (frequent spasms of small arteries induced by temperature changes and emotion resulting in deprivation of blood supply to peripheral tissues), CREST syndrome (calcium deposits, Reynaud's syndrome, loss of muscular control of the esophagus, sclerodactylia, and telangiectasia), and Sjogren's syndrome (inflammation of the conductive, cornea, tear, and salivary glands with progressive destruction by lymphocytes and plasma cells) are both subcategories of scleroderma.

The clinical manifestations of scleroderma include the following symptoms: fatigue, swelling and numbness of the hands and feet, shiny skin and disappearance of skin folds, ulcers on the fingers, calcium deposits on the fingers, joint inflammation, joints tightening into bend position, muscle weakness, itchy skin, difficulty in swallowing, shortness of breath, fatty diarrhea or constipation, and loss of body hair. Although ultimately renal impairment and failure is a common endpoint, therapy affecting the hypertensive phase or renal involvement has changed the mortality rate.

Diabetes Mellitus type I

This form of diabetes involves the chronic inflammatory destruction of the insulin-producing islet cells of the pancreas. Although this form of diabetes is treated similarly to the type II form (which is not linked to autoimmunity), i.e. insulin replacement therapy, early identification of type I versus type II individuals may be useful to thwart the autoimmune destruction of the β -cells. There are an estimated 500,000 to 1 million Americans that have type I diabetes, it is the seventh leading cause of death, and the following is a list of the progressive complications that are associated with the unregulated carbohydrate balance in tissues: retinopathy leading to blindness, nephropathy (diabetic nephropathy is the leading cause of end-stage renal disease), coronary and cardiovascular disease, neuropathy (severe forms can lead to amputation), impotence (diabetic neuropathy and cardiovascular disease can lead to impotence), and stroke.

Sarcoidosis

Sarcoidosis is a granulomatous disorder characterized by enhanced cellular immune response at one or more involved sites. The prevalence of sarcoidosis is 5 in 100,000, so approximately 13,000 patients have been diagnosed. Between 80-90% of patients with sarcoidosis have pulmonary involvement, however, any organ can be affected. Pulmonary involvement includes dyspnea with or without exertion, persistent dry cough, and atypical chest pain. Cor pulmonale can develop as a complication of pulmonary dysfunction and further progress to right atria dilatation

and right ventricular hypertrophy. Ocular involvement includes disturbance in visual acuity, and in chronic cases may lead to glaucoma, cataract formation and retinal neovascularization. In 80% of the cases, sarcoidosis is self-limiting and results in minimal symptomology, discomfort, or debilitation. However in the remaining 20%, sarcoidosis patients face potentially serious debilitation, disfigurement, and can be life threatening. Misdiagnosis is frequent and can limit appropriate therapeutic intervention.

Nephritis

Inflammation of the kidneys results in impaired renal function. Nephritis can be either interstitial or glomerular. In either case, mononuclear cells infiltrate in the interstitium of the renal cortex. Eosinophils, and in some cases, polymorphonuclear leukocytes are found in a similar compartment. The infiltrate may be diffuse or patchy and may be accompanied by fibrotic tissue. Membranous nephropathy may develop and lead to impairment of glomerular filtration rate. There is evidence to suggest both cytotoxic T cells and T-cell mediate delayed hypersensitivity are involved. Nephritis is a component of the clinical manifestation of systemic lupus erythematosis, scleroderma, and other autoimmune diseases and disorders.

Current therapy for Autoimmune Diseases and Disorders

Agents used to treat autoimmune disease fall into one of the following four categories: analgesics (NSAIDs, salicylates), immunosuppressive agents, hormones (glucocorticoids), and skin and mucosal membrane preparations

Analgesics: Typically, pain associated with autoimmune disease can be controlled with NSAIDs including but not excluded to, salicylates, para-aminophenol derivatives, indole and indene derivatives, heteroaryl acetic acids, arylpropionic acids, anthranilic acids, enolic acids, or alkanones. Antiinflammatory agents such as cyclooxygenase inhibitors, lipoxigenase inhibitors, and others can be used to block the inflammation physiological pathway which mediate pain. However, because these drugs are limited in their efficacy in advanced or more severe stages of autoimmune disease, these agents are add-on therapies.

NSAIDs derive their principle mechanism of action by the inhibition of prostaglandin and leukotriene synthesis. These compounds inhibit key enzymes in the biosynthetic pathway, i.e. cyclooxygenase. There are drugs that selectively inhibit isoforms of cyclooxygenase 1 and 2 (COX-1, COX-2) which enhances patient tolerance due to the prevalence of COX-2 induction occurs in inflammation mediated by cytokines and others.

Immunosuppressive drugs or agents: Agents involved in the modification of the immune system for the treatment of autoimmune disease are immunosuppressive

agents. Immunosuppressives include azathioprine, cyclosporine, penicillamine, antimalarials (chloroquine, hydroxychloroquine), alkylating agents (cyclophosphamide), and antimetabolites (methotrexate).

Hormones and Growth Factors: Agents acting at hormone receptors or growth factor receptors include steroids (glucocorticoids), adrenocorticotrophic hormone (corticotropin), and tumor necrosis factor inhibitors (soluble TNF receptors (enbrel) and TNF monoclonal antibody (remicade). Since the autoimmunity component of the disease is driven primarily by activated T-cells, which give rise to cytokines IL-1 and TNF at the affected areas. These agents are known to interfere with the actions of these cytokines.

Corticosteroids affect the immune response by decreasing growth and development of mast cells, inducing apoptosis, suppressing lymphocyte generation of IL-5 and other cytokines, inhibiting some mediator release, inhibiting cytokine production, inhibiting the transcription of cytokines (for example IL-8, TNF- α , prototypic antiviral chemokine (regulated-on-activation normal T-expressed and secreted, RANTES), and GM-CSF), and inhibiting nitric oxide synthesis.

Plasma Exchange: A useful technique for the removal of autoantibodies is a process called plasmaphoresis or plasma exchange. In this process, antibodies are removed that mediate humoral immune response to the autoantigen.

Antioxidants: Many of the therapies in use for these autoimmune diseases are aimed at reducing the level and extent of tissue damage mediated by T-cell immune response. For example, dimethyl sulfoxide, dimethyl sulfone, para-aminobenzoic acid, and vitamin E are included in this category.

Limitations Current Therapies for Autoimmune Disease based upon Low efficacy

The therapies discussed above are limited to the slowing or retarding the progression of autoimmune disease. As immune response tissue damage occurs, degeneration of the function progresses, irreversible damage occurs, and therapeutic options become limited. Thus, therapies for autoimmune disease are aimed at reduction of manifestation of symptoms by controlling the clinical manifestations of inflammation and the hypersensitive immune response.

The reduction of clinical symptoms of autoimmune disease following immunosuppressive therapy by one of the agents listed above is only evident after several weeks to months after therapy. The slow clinical relevance of these therapies limits the clinician to determine optimal therapy for individuals with autoimmune disease, and provides a risk for selection of optimal therapy for any given stage of the disease. Furthermore, there may be delays in identifying those

patients that have an autoimmune hyperreactivity, and this can delay therapeutic intervention.

5 Limitations Current Therapies for Autoimmune Disease based upon Toxicity or Undesired side effects

There are toxicities and undesired side effects associated with the above current therapies for autoimmune disease that require monitoring. Drugs used to treat autoimmune disease may cause death, disability, disease, and place an unborn child at risk. The undesired side effects or toxicities are listed for each drug category as described above.

Analgesics associated side effects include dyspepsia, gastric or small bowel bleeding, ulceration, renal insufficiency, confusion, rash, headache, hepatic toxicity. NSAIDs also reversibly inhibit platelet aggregation and prolong bleeding time.

Immunosuppressive therapies have associated side effects including antimalarials: retinal or macular damage; sulfonamides: hematologic toxicities (leukopenia, thrombocytopenia, hemolysis in patients with glucose 6-phosphate dehydrogenase (G6PD) deficiency); antimetabolites: hepatic compromise including hepatic fibrosis, ascites, esophageal varices, cirrhosis, pneumonitis, myelosuppression; immunosuppressives: myelosuppression, (cyclosporine: renal insufficiency anemia, hypertension); penicillamine: rash, stomatitis, dysgeusia or metallic taste, myelosuppression (thrombocytopenia), proteinuria, nephrotic syndrome or renal failure, and induction of autoimmune syndromes (systemic lupus erythmatosus, myesthenia gravis, polymyocytis, Goodpasture's syndrome).

Glucocorticoid associated side effects include increased appetite, weight gain, fluid retention, acne, ecchymosis, development of cushoid facies, hypertension, hyperkalemia, diabetes, hyperglycemia, hyperosmolar state, hyperlipidemia, hepatic steatosis, atherosclerosis, myopathy, aseptic necrosis, osteoporosis, ulcers, pancreatitis, psuedotumor cerebri, psychosis, glaucoma, cataract formation, vascular necrosis, increased suseptibility to infection, impairment of the hypothalamus-pituitary axis, decreased thyroid hormone serum binding protiens, and impaired wound healing.

Since the majority of autoimmune disease patients are women in their reproductive years, the level and extent the agents used to treat autoimmune disease affects or has a potential to affect the mother during pregnancy, cross the placenta, affect the developing fetus, or be excreted in breast milk during lactation are important issues facing the skilled practitioner. Clinical medical therapeutic decisions must weigh the use of all of the above current therapies for autoimmune disease against known capacity of these agents to affect both the mother and the child.

Description of Mechanism of Action Hypotheses for Future Drug Development for the Treatment of Autoimmune Disease

Autoimmune disease has been thought to be the result of host genetic factors, immunoregulatory abnormalities and autoimmunity, and triggering or persistent microbial infection.

A gene, genes, or gene pathway involved in the etiology of autoimmune diseases or disorders or associated disorders or potential sites for targeted drug therapy of autoimmunity are depicted in Table 9 with the specific gene list in Table 4. Current candidate therapeutic interventions in development are listed for the treatment of autoimmune disease or disorder, Tables 40 and 42, and for systemic lupus erythematosus, Table 41.

D. Immunosuppression- Transplantation

Description of Transplantation

There are many different conditions in which medical or surgical therapy is unable to halt, retard, or treat the underlying disease, disorder, or dysfunction. Although many refractory diseases, disorders, or dysfunctions do not lead to severe cases, there are some in which the progression leads to conditions in which the remaining therapeutic alternative is replacement of the diseased tissue with normal donated tissue by transplantation. These end stage conditions include both primary disease or complications from a disease. For example whole organ transplantation is an end-stage therapeutic alternative in the following indications, end-stage cardiomyopathy, end-stage renal disease, pulmonary disease, cirrhosis of the liver, as well as other end-stage diseases affecting whole organ function.

Besides whole, or partial organ transplantation there are programs aimed at replacing cells in specific tissues to enable or restore physiologic function. For example cellular transplantation includes, but not excluded to, grafting bone marrow cells in patients with hematopoietic or lymphocytic cancers, dopaminergic producing cells in brains of patients with Parkinson's disease, striated muscle cells in patient's with Duchenne's muscular dystrophy, myocytes or cardiomyocytes in patient's with ischemic heart disease or cardiomyopathy, and replacement of neurons or astrocytes or glial cells in neurodegenerative disease including but not excluded to Alzheimer's disease, amyotrophic lateral sclerosis, multiple sclerosis, Huntington's disease, refractory pain, epilepsy, and stroke.

In this way, transplantation includes autografts, isografts, allografts or xenografts and can involve whole organ or cellular grafts. With the exception of autologous transplantation, all other transplantation procedures include pre- and

post-surgical immunosuppression to blunt graft rejection or graft versus host disease. Successful immunosuppression in this setting includes an appropriate balance between the need to prevent the process of graft rejection and the risk of suppressing the recipient's immune system to the extent that they become vulnerable to infection or other complications.

Transplantation is immunologically mediated. Both T cells and circulating antibodies are induced against allografts or xenografts. While the antibodies are responsible for rejection of erythrocytes, T-cells are mainly responsible for the rejection of most other type of tissue. The antigens found on grafted tissue which initiate the rapid rejection of an allograft are found on most cell membranes and are encoded by genes in the major histocompatibility complex (MHC) which are called the HLA. The structures encoded in these genes, MHC class I and class II molecules, are involved in the determining the discrimination between self and non-self. The degree of the histocompatibility between donor and recipient can be determined serologically, by genotyping, or by a mixed lymphocyte reaction. Survival of HLA nonmatched allografts is prolonged by anti-inflammatory agents, cytotoxic agents, antimetabolites, and other modalities aimed at immunosuppressing the recipient. These approaches have proven clinical success in terms of graft survival and clinical symptomology.

Rejection can occur at any time, and is either hyperacute, acute or delayed. The rate, extent, and underlying mechanism of transplantation rejection varies dramatically from individual to individual. Physiological factors include patency of blood circulation, lymphatic drainage, expression of antigens on the graft, and others that can influence the rejection rate.

In hyperacute rejection, preexisting host antibodies to antigens found on the grafted tissue mount an immune response. These antibodies activate complement, followed by platelet activation and deposition causing swelling and interstitial hemorrhage in a whole organ graft, or specific cell targeting in a cellular transplant. Cell mediated immunity is not activated in the hyperacute response.

In acute rejection, infiltration of lymphocytes and macrophages recognize the foreign antigen on the graft cells, and initiate a cascade of intragraft events that ultimately leads to host cellular and humoral mediated destruction of the grafted tissue and if unchecked will result in irreversible loss of the graft. This acute process occurs rapidly and does not in the first stages affect the vital structures of a whole organ graft, which allows for identification of the process and implementation of therapy. In many cases, an acute rejection episode can be reversed, and approximately 30-50% of whole organ graft recipients undergo one or more of these episodes in the early transplant period.

Delayed or chronic rejection occurs in a slower process than acute rejection and ultimately leads to a gradual loss of function in the grafted tissues. In chronic or delayed rejection, both cell mediated immunity and humoral immunity is activated. Chronic rejection is characterized by arteriosclerosis, in which the smooth muscle cells lining the arteries in the graft organ proliferate to create lesions and lead to fibrosis, with a result of constricting blood flow. As a result of the chronic immune rejection, there is slow and progressive destruction of the grafted organ or cells. If damage to the tissue is extensive, very little can be done to save the graft.

Current Immunosuppressive Therapies

The goal of clinical immunosuppression in the transplantation setting is to control allograft rejection. Clinical immunosuppression involves the non-specific suppression of both cell-mediated and humoral immune reactivity to the grafted tissue. Although a number of methods have been proposed, successful prolongation of graft survival has been attained through the use of a combination of therapies that suppress both the lymphocytic interaction and proliferation and therapies that deplete the pool of available lymphocytes.

Antiproliferative agents

These agents are useful to blunt the proliferative phase of lymphocyte activation of the immune response.

Purine analogs

Azathioprine acts to inhibit the proliferation of T cells. Azathioprine is cleaved to 6-mercaptopurine and it is this active compound that serves to suppress the T-cell mediated antigenic determination and engraftment. Azathioprine is a relatively non-selective immunosuppressive agent. Other agents in the same class as azathioprine, i.e. antimetabolites, include but are not excluded to, mercaptopurine, chlorambucil, and cyclophosphamide.

Pyrimidine analogs

The agents (cytosine arabinoside) inhibits DNA synthesis and therefore have their greatest effect on the immune response during the proliferative phase of lymphocyte activation. These agents inhibit primary antibody response and have minimal effects on the cell-mediated immunity.

Folic acid analogs

These agents (methotrexate, aminopterin) inhibit dihydrofolate reductase preventing the conversion of folic acid to tetrahydrofolic acid. This conversion is necessary for the production of DNA and RNA.

Alkylating Agents

These agents (nitrogen mustard, phenylalanine mustard, busulfan, cyclophosphamide) alter the structure of the DNA and RNA. These agents have reactive ring structures which combine with electron rich groups such as tertiary nitrogen in purines or pyrimidines, or -NH₂, -COOH, -SH, -PO₃H₂ groups. These reactions alter the composition of the DNA, and if not repaired, chromosomal replication will be altered in activated proliferating cells. The use of alkylating agents in the setting of transplantation is time dependent and is effective just before or during the activation of the immune system by antigen. Cyclophosphamide has been shown to have a greater effect on B-cells rather than T-cells, thereby inhibiting the humoral response to a greater degree.

Antibiotics

These agents (actinomycin D, mitomycin C, puramycin, chloramphenicol) inhibit either nucleic acid or protein synthesis.

Cyclosporin acts by inhibiting the production of IL-2, which results in an inhibition of the proliferation of T and B lymphocytes. Cyclosporin is widely prescribed for transplantation patients due to the clinical advantage of potent immunosuppression with limited myelosuppression.

FK-506 (Tacrolimus) is an agent that acts by inhibiting the production of IL-2 which prevents the proliferation of T and B lymphocytes.

Mycophenolate mofetil is rapidly converted to mycophenolic acid which selectively inhibits T and B cell proliferation. Mycophenolate mofetil has an advantage over azathioprine because it does not damage chromosomes.

Lymphocyte Depletion agents

Antilymphocytic globulin (ALG) is an agent that binds to circulating T-lymphocytes and the cells coated with the ALG are lysed and cleared by the reticuloendothelial system. ALG is more commonly used for renal transplantation, showing little to no benefit for liver or bone marrow transplantation..

Radiation

Total lymphoid irradiation or total body irradiation is based upon the immunosuppression observed after this procedure was used in patients with Hodgkin's lymphoma. The radiation causes breakdown in the nucleic acid structure, and the effect is time dependent since there are systems within all cells for the repair of DNA. Since the radiation affects those cells in M or G₂ phase, those cells in G₁ or S phase are resistant.

Monoclonal antibodies

A murine monoclonal antibody is available to deplete the circulating CD3 lymphocytes. This antibody reacts with the T3 recognition site of the T-lymphocytes and blocks the recognition of the Class I and II antigens. This leads to

prevention of the activation of the effector lymphocytes. This antibody has been useful in the treatment of rejection of renal, pancreatic, hepatic, cardiac, and pulmonary whole organ transplantations.

Steroids- such as the glucocorticoids are widely used in transplantation in combination with other drugs. As well as providing antiinflammatory therapy, corticosteroids suppress immune function by inhibiting the activation of T cells. Corticosteroids affect the inflammation within the airways by decreasing growth and development of mast cells, inducing apoptosis, suppressing lymphocyte generation of IL-5 and other cytokines, inhibiting some mediator release, inhibiting cytokine production, inhibiting the transcription of cytokines (for example IL-8, TNF- α , prototypic antiviral chemokine (regulated-on-activation normal T-expressed and secreted, RANTES), and GM-CSF), and inhibiting nitric oxide synthesis. Steroids are highly effective in the early induction and maintenance regimens and are first line therapy in acute allograft rejection.

Blood transfusions can be used to cause allosensitization if the recipient is exposed to donor antigens in the presence of azathioprine. In this way, induction of a specific degree of hyporeactivity against graft antigens can result by a potential suppressor cell phenomena.

Limitations of Immunosuppressive Therapies due to Lack of Efficacy

As suggested, the efficacy of immunosuppression is a balance between prevention of graft rejection or graft versus host disease and subjecting a patient unnecessarily to blunted immune defenses to ward off infections. All too often, this balance is not achieved and on one end the patient succumbs to infections or on the other the graft is rejected. It has been estimated that 30% of the transplantation patients are in this category.

Limitations of Immunosuppressive Therapies due to Toxicities or Undesired Side Effects

Antiproliferative Agents

Azathioprine is associated with suppression of bone marrow production, and blood disorders including anemia, thrombocytopenia, and leukopenia.

Hepatotoxicity occurs in a dose-independent manner, and is irreversible.

Azathioprine is associated with chromosome damage and therefore is mutagenic.

Methotrexate and aminopterin are associated with bone marrow suppression, mucosal breakdown, gastrointestinal bleeding, megaloblastic hematopoiesis.

Alkylating Agents are associated with stomatitis, nausea, vomiting, diarrhea, skin rash, anemia, and alopecia. Specifically, cyclophosphamide has been associated with fluid retention, hemorrhagic cystitis, and cardiac toxicity.

5 Cyclosporin is associated with gingival hyperplasia, hirsutism, tremor, hypertension, hyperkalemia, hepatotoxicity, hyperglycemia, hypomagnesiumemia, hypercholesterolemia, hypertriglyceridemia, and hyperuricemia, nausea and gastrointestinal irregularities, and renal dysfunction. Nephrotoxicity associated with cyclosporin manifests as tubular necrosis, interstitial fibrosis, and tubular atrophy.

10 FK506 is associated with neurotoxicity, nephrotoxicity, and disturbances of glucose metabolism. The major neurotoxic symptoms are reversible and dose dependent and include headache, tremors, parasthesias, insomnia, increased sensitivity to light, mood changes, aphasia, and seizures. There has been a suggested association of FK-506 with cardiomyopathy and it is contraindicated in pregnancy.

15 Lymphocyte Depletion Agents

ALGs are associated with anemia, thrombocytopenia, and allergic reactions including urticaria, anaphylactoid reactions, serum sickness, joint pain, fever, and malaise.

20 Radiation is associated with higher incidence of infections and chromosomal breakage and mutations.

Monoclonal antibody therapy has been associated with the production of human anti-mouse antibodies (HAMA) in 80% of the treated patients and the sensitization rate is 15-40% thus limiting retreatment rates. Side effects are fever, chills, nausea, vomiting, headache, dyspnea, wheezing, pulmonary edema, 25 tachycardia, hypotension, aseptic meningitis, seizures, and coma. These symptoms are related to the inordinate release of cytokines TNF, IL-1, and interferon-gamma. Although these symptoms can be reduced by pretreatment with steroids, acetaminophen, or diphenhydramine the HAMA response precludes repeated use.

30 Steroids- Glucocorticoid associated side effects include increased appetite, weight gain, fluid retention, acne, ecchymosis, development of cushoid facies, hypertension, hyperkalemia, diabetes, hyperglycemia, hyperosmolar state, hyperlipidemia, hepatic steatosis, atherosclerosis, myopathy, aseptic necrosis, osteoporosis, ulcers, pancreatitis, pseudotumor cerebri, psychosis, glaucoma, cataract formation, vascular necrosis, increased susceptibility to infection, impairment 35 of the hypothalamus-pituitary axis, decreased thyroid hormone serum binding proteins, and impaired wound healing.

Complications of Immunosuppression

In addition to the above listed toxicities and undesirable side effects, potent immunosuppression as required in the transplantation setting leads to prolonged immune compromise and predisposes the patient to infections (80% of the patients) and cancer (ranging between 10-40% of the patients). This risk has been proposed to result from impaired immune surveillance mechanisms, chronic antigenic stimulation, reactivation of latent oncogenic viruses and the direct oncogenic effects of the immunosuppressive agents.

Moreover, 40% of the deaths of transplant patients are attributable to the complications of infections or a combination of infection and graft rejection. The infections experienced by transplant patients are 50% bacterial, 30% viral, 15% fungal. Some of the common bacterial infections are Staphylococcus aureus, Staphylococcus epidermidis, and gram-negative rods in line sepsis. Urinary tract infections, pneumonias, wound infections, and surgical infections (including cholecystitis, appendicitis, diverticular disease, ulcer, etc.). Common viral infections include cytomegalovirus, Epstein-Barr virus, Herpes Simplex Virus, and varicella zoster virus. Further, common fungal or protozoan infections include Candida albicans, Asperigillus flavus, Cryptococcus neoformans, Coccidioides immitis, Histoplasma capsulatum, Norcardia asteroides, and Pneumocystis carinii.

Description of Mechanism of Action Hypotheses for Future Immunosuppressive Drug Development

The majority of the hypotheses for future therapeutic interventions for graft rejection and graft immunoreactivity are based upon the understanding the immunologic mechanisms that cause and perpetuate the rejection within the graft.

A gene, genes, or gene pathway involved in the etiology of transplantation or immunosuppression or associated disorders or potential sites for targeted drug therapy of transplantation are depicted in Table 9 with the specific gene list in Table 4. Current candidate therapeutic interventions in development for the treatment of anemia are listed in Tables 42 and 43.

E. Pain Associated with Inflammation

Description of Pain Associated with Inflammation

Pain associated with inflammation can be caused by pathologic processes in somatic structures or viscera, or by prolonged dysfunction of parts the peripheral nervous system.. Pain associated with inflammation may be the result of recurrent injuries, trauma, headache, arthritis, chronic obstructive pulmonary disease, psoriasis, or other pathologies. Pain associated with inflammation may be acute or chronic depending on the level and extent of the inflammation.

Current therapies for Pain Associated with Inflammation

Therapeutic management of pain resulting from inflammation includes a three step ladder approach: non-opioid analgesics are stepwise prescribed in combination with moderate to potent opiates. The guidelines call for a determination by the patient and the physician of pain relief. Broadly speaking, the guidelines are as follows: mild pain is treated with non-opioid analgesics, moderate or persisting pain is treated with a weak opioid plus non-opioid analgesics, and severe pain that persists or increases is treated with a potent opioid plus non-opioid analgesics.

Analgesics: Typically, pain associated with inflammation can be controlled with NSAIDs including but not excluded to, salicylates, para-aminophenol derivatives, indole and indene derivatives, heteroaryl acetic acids, arylpropionic acids, anthranilic acids, enolic acids, or alkanones. Antiinflammatory agents such as cyclooxygenase inhibitors, lipoxygenase inhibitors, and others can be used to block the inflammation physiological pathway which mediate pain and the progression of the disease. However, because these drugs are limited in their efficacy in advanced or more severe stages of arthritis, these agents are add-on therapies.

NSAIDs derive their principle mechanism of action by the inhibition of prostaglandin and leukotriene synthesis. These compounds inhibit key enzymes in the biosynthetic pathway, i.e. cyclooxygenase. There are drugs that selectively inhibit isoforms of cyclooxygenase 1 and 2 (COX-1, COX-2) which enhances patient tolerance due to the prevalence of COX-2 induction occurs in inflammation mediated by cytokines and others.

Further, pyrimidine synthesis inhibitors can be used as an antiinflammatory agent in arthritis, e.g. leflunomide.

Limitations of Current Therapies for Pain Associated with Inflammation

Limitation of Therapies for Pain Associated with Inflammation due to Low efficacy

The therapies discussed above are limited to the slowing or retarding the progression of arthritis. As degeneration of the joints progresses, and irreversible damage occurs, the options become limited. Thus, therapies for arthritis are aimed at reduction of manifestation of symptoms by controlling the clinical manifestations of inflammation.

Limitations of Therapies of Pain Associated with Inflammation due too Toxicity or Undesired side effects

Analgesics associated side effects include dyspepsia, gastric or small bowel bleeding, ulceration, renal insufficiency, confusion, rash, headache, hepatic toxicity. NSAIDs also reversibly inhibit platelet aggregation and prolong bleeding time.

5 Description of Mechanism of Action Hypotheses for Future Pain Associated with Inflammation Drug Development

10 The persistence of pain most likely involves a cascade of pathological neurochemical events that lead to abnormal sensory hyperexcitability and excitotoxicity. The genes listed in Figure 1 are part of a pathway are all involved in producing prostaglandins or leukotrienes, which are two potent mediators of inflammation. Inordinate levels of prostaglandins have been implicated in pain associated with inflammation, and several drugs target this branch of the pathway, to inhibit the action of leukotrienes. When a cell receives a pro-inflammatory stimulus, such as tumor necrosis factor, membrane phospholipids, or interleukin-1, as shown in 15 the figure, membrane phospholipases are activated, and arachidonic acid is released from membrane phospholipids into the cell. The liberated arachidonic acid is then metabolized either by the cyclooxygenase enzymes, which leads to the production of prostaglandins, or the lipoxgenase family of enzymes, which leads to the production of leukotrienes. There are several types of prostaglandins and leukotrienes, and many of the enzymes listed here function to convert one form into another. 20

The presence of leukotrienes and prostaglandins can lead to a persistence of neural hyperexcitability involving a sequence of neuroplastic events.

25 A gene, genes, or gene pathway involved in the etiology of pain or associated disorders or potential sites for targeted drug therapy of pain are depicted in Table 9 with the specific gene list in Table 4. Current candidate therapeutic interventions in development for the treatment of pain associated with inflammation are listed in Table 44.

30 F. Psoriasis

Description of Psoriasis

Papulosquamous skin disorders have diverse etiologies and include psoriasis, Reiter's syndrome, pityriasis rosea, lichen planus, oityriasis rubra pilaris, secondary syphilis, mycosis fungoides, and ichthyosiform eruptions.

35 Psoriasis is a genetically determined, chronic epidermal proliferative disease with an unpredicable course. Psoriasis appears as erythematous plaques with silvery, mica-like scales, and is usually nonpruritic. The plaques appear anywhere on the body and almost never involves the mucous membranes. There are variations of psoriasis including guttate psoriasis, inverse psoriasis, pustular psoriasis,

erythroderma, and psoriatic arthritis. There is an increased prevalence of psoriasis in subjects with the HLA antigens BW17, B13, and BW37. Further, 30% of cases have a family history of psoriasis. The Koebner phenomena is a hallmark characteristic of psoriasis, e.g. intense trauma (scratches or surgical incisions) to the skin induces new linear papulosquamous lesions.

This multifactorial disease is characterized by an accelerated cell cycle in an increased number of dividing cells that results in rapid epidermal cell proliferation. It is estimated that 4-5 million Americans have psoriasis, 100,000 have severe cases, and 1 in 20 have psoriatic arthritis.

Current Therapies for Psoriasis

The goals of the therapeutic regimens is to limit the epidermal proliferation underlying the dermal inflammation. There are both topical and systemic treatments available, however in either category the treatment suppresses the condition for only as long as is administered. The treatment of psoriasis entails a stepwise increase of extent of the therapy ranging from topical applications to phototherapy to systemic interventions to prevent the epidermal proliferation.

In the first step topical treatments include corticosteroid ointments, vitamin D containing ointments, preparations containing coal tar or anthralin, salicylic acid containing ointments, and various other moisturizers and bath solutions. These steps are aimed at reducing the itching, scaling, and progression of the lesions.

In the second step, phototherapy other than natural sunlight can be used to thwart the epidermal cell proliferation. In these cases, ultraviolet light is administered to affected areas or uniformly to the body. In phototherapy, light delivered to the skin activates porphyrin molecules. These activated molecules transfer their energy to form cytotoxic singlet oxygen leading to lethal alteration of cellular membranes and subsequent tissue destruction. In UVB therapy, UVB light is administered alone or with ointments containing coal tar, anthralin, or salicylic acid. UVA light is administered with psoralen.

In the third step of therapeutic regimens for psoriasis, systemic agents are administered to those cases refractory to the previously described first two steps. These compounds include retinoids, methotrexate, hydroxyurea, cyclosporin, azathioprine, 5-fluorouracil, cyclophosphamide, vinblastine, dapsone, and sulfasalazine.

Limitations of Current Therapies for Psoriasis

The main limitation of the current therapies for psoriasis is that the drugs are only efficacious during the administration. Further, periods of remission and

outbreaks are difficult to impossible to predict. It has been shown that patients must rotate their treatments to retain efficacy. This can lead to missed schedules and requires patient education. Lastly, for all the listed therapies there is unreliable efficacy in their ability to stop proliferation and inflammation of the lesions.

5 Toxicities of the current therapies include the following: phototherapy can lead to other skin lesions and sunburn. Cytotoxic agents used as immunosuppressive agents including methotrexate, 5-fluorouracil, cyclophosphamide, and vinblastine have associated side effects including hepatic compromise including hepatic fibrosis, ascites, esophageal varices, cirrhosis, pneumonitis, myelosuppression,
10 (cyclosporine: renal insufficiency anemia, hypertension).

 A gene, genes, or gene pathway involved in the etiology of psoriasis or associated disorders or potential sites for targeted drug therapy of psoriasis are depicted in Table 9 with the specific gene list in Table 4. Current candidate therapeutic interventions in development for the treatment of psoriasis are listed in
15 Table 45.

G. Atherosclerosis

Description and Potential Intervention of Atherosclerosis

 Atherosclerosis is a complex combination of hyperlipidemia, injury to the
20 endothelium, and inflammation. The interaction of these multiple processes in association with local genetic and hemodynamic influences may promote the formation of atheromatous plaques as a reparative response of the arterial wall. Atherosclerotic plaques are composed of thrombogenic lipid-rich core protected by a fibrous cap comprising smooth muscle cells and inflammatory cells. The
25 inflammatory cells are predominantly macrophages. As atherosclerotic plaques build blood flow is reduced creating ischemia in tissues down stream from the area of the plaque.

 In another model, the stenosis created by the plaques may be a part of the resulting ischemic event. Frequently, less obstructive but more vulnerable plaques
30 occur which are characterized by a thinned fibrous cap, marked lipid accumulation, a large number of macrophages, and a smaller amount of smooth muscle cells. It has been proposed that since these plaques are more prone to rupture creating contact with the highly thrombogenic materials of the lipid-rich nucleus of these lesions, thrombosis is stimulated.

35 Advanced atherosclerotic lesions are caused by a series of cellular and molecular events involving replication of smooth muscle cells and macrophages on the vessel wall. The interaction of these cells with the T lymphocytes can lead to a fibroproliferative response. Large amounts of connective tissue produced by these

smooth muscle cells consist of macrophages, T lymphocytes, smooth muscle cells, connective tissue, necrotic residues, and varying amounts of lipids and lipoproteins.

Endothelial cells maintain the vessel surface in a non-thrombogenic state, preventing platelet and leukocyte adhesion, and act in maintaining the vascular tonus by releasing nitric oxide, prostaglandin, and endothelin. These cells also produce growth factors, cytokines, and chemokines to maintain the integrity of the collagen- and proteoglycan-rich basement membrane. Changes in some of these functions may trigger cell interactions with monocytes, platelets, smooth muscle cells, and lymphocytes. Hyperlipidemia and hypercholesterolemia are sufficient to induce dysfunction of the endothelial modulation of the vasoactive reactions and arteriolar tonus.

The inflammatory mechanisms involved in the initial events or atherosclerosis are classic components of a specialized type of chronic inflammatory response that precedes the migration and proliferation of smooth muscle cells of the vessel wall. The formation and accumulation of foam cells in the intima leads to the first stage of the atherosclerotic lesion. In this stage, the accumulation of fatty striae consisting of a mixture of macrophages, lipids, and T lymphocytes representing a purely inflammatory response. If the stimulating agent is maintained, i.e. hyperlipidemia, hypercholesterolemia, or other risk factor, then the protective inflammatory response will also persist and may become deleterious to the cells lining the arterial wall. This condition may lead to an intermediate lesion that may contain multiple smooth muscle cell layers, macrophages, and T lymphocytes. A fibrous capsule is formed covering the contents of the lesion.

There is evidence to suggest that the inflammatory process and specific immune mechanisms are involved in atherogenesis. At sites close to the plaque rupture, inflammatory processes are observed resulting from T cell-dependent autoimmune response. This may lead to inflammatory reactions participating in the destabilization of the fibrous cap. Immunoglobulins, T lymphocytes, and macrophages are found in the plaques. B lymphocytes and plasmacytes may also be detected in the adventitia adjacent to the plaques. Autoimmune reactions against the oxidized lipoproteins have been observed. The macrophages are transformed into foam cells and in the presence of LDL, form immunocomplexes with the LDL by Fc fragments of the immunoglobulins. These LDL immunocomplexes can induce numerous metabolic and functional changes which can directly or indirectly damage the endothelial cells leading to the progression of the atherosclerotic lesion.

Despite the evidence of the involvement of the immune system in atherogenesis, the complexity of the immune reactions and response impairs the clarification of the involvement of these mechanisms at the various stages of

atherosclerosis. The sequence of immune response event suggests an initial mechanism to respond to injury. However, this protective inflammatory response in the presence of persistent stimulus and the formation of a fibroproliferative response can be amplified.

5 Attempts to modify the specific cell interactions with growth factor mediators or intracellular signalling molecules has provided a window to the potential prevention or regression of the lesions.

 A gene, genes, or gene pathway involved in the etiology of atherosclerosis or associated disorders or potential sites for targeted drug therapy of atherosclerosis are depicted in Table 9 with the specific gene list in Table 4. Current candidate
10 therapeutic interventions in development for the treatment of atherosclerosis are listed in Table 46.

Endocrine and Metabolic Disease

15 Included in the description below are endocrinologic and/or metabolic diseases, disorders, or syndromes. They include diabetes, diabetes insipidus, obesity, contraception (not a disease but a common reason for taking steroid drugs), infertility, hormonal insufficiency related to aging, osteoporosis, acne, alopecia, adrenal dysfunction, thyroid dysfunction, and parathyroid dysfunction. Application
20 of the methods of this invention to these diseases is described.

A. Diabetes Mellitus

 Carbohydrate metabolism in mammals is controlled by a unique interplay of hormones, neurotransmitters, and other physiological influences to ensure a constant
25 supply of metabolic fuel is available to the tissues. The two main hormones that regulate carbohydrate balance are insulin and glucagon. Both hormones are produced in the pancreas; β -cells produce insulin, α -cells produce glucagon. Insulin in the fuel excess state stimulates storage of the available metabolic precursors into glycogen and lipids; glucagon in the fuel deficient state stimulates the movement of
30 the fuel stores to available metabolic precursors. When regulation of insulin or glucagon is abnormal there are pathologic changes.

 Type II Diabetes (Diabetes Mellitus; DM) is a heterogeneous disorder of carbohydrate metabolism characterized by absolute or relative insulin deficiency alone or in combination with insulin resistance (sensitivity). DM is associated with
35 hyperglycemia and consequent polyuria and polydipsia.

 There are two forms of the disease, insulin-dependent diabetes mellitus (IDDM) which accounts for approximately 10% of the DM cases in the United States, and non-insulin-dependent diabetes mellitus (NIDDM) which accounts for

the remaining diagnosed cases. The incidence rate for all cases of DM in the U.S. is approximately 440 per 100,000. Type I (juvenile onset) diabetics produce little or no insulin and may be severely hyperglycemic if untreated. They are entirely dependent on exogenous insulin administration.. NIDDM (maturity or adult onset, nonketotic DM) patients retain significant capacity to secrete insulin, do not exhibit ketosis, and are not dependent on exogenous insulin for immediate survival. Within the pancreas, the β -islets cells are lost, stop producing or secreting insulin in patients with IDDM, but remain functional in patients with early stage NIDDM. In both cases of DM, glucagon opposes the effect of insulin on the liver by stimulating glycogenolysis and gluconeogenesis, but glucagon has little if no effect on the peripheral utilization of glucose. In the diabetic patient with insulin deficiency or insulin resistance and hyperglucagonemia, there is an increase in hepatic glucose production, a decrease of peripheral glucose uptake, and a decrease in the conversion of glucose to glycogen in the liver.

Broadly, the physiologic changes stimulated by insulin, the primary hormone responsible for specific uptake of glucose from the periphery to tissues, is to increase the available storage of glucose into glycogen stores. In the liver, insulin stimulates the uptake and storage of glucose as glycogen, and inhibits hepatic gluconeogenesis and glycogenolysis. In skeletal muscle, insulin stimulates glucose uptake and storage as glycogen and amino acids in protein and inhibits release of gluconeogenic precursors (e.g., alanine, lactate and pyruvate) to the hepatic circulation. In adipose tissue, insulin stimulates the glucose uptake and metabolism to glycerol (the backbone of triglycerides for storage in fat droplets) and inhibits the flow of gluconeogenic precursors to the hepatic circulation, e.g. glycerol and nonesterified fatty acids. Insulin inhibits the breakdown of triglycerides, glycogen, protein and the conversion of amino acids to glucose (gluconeogenesis).

In the intracellular process of storage of glucose as glycogen in the liver, insulin stimulates the glycogen synthase complex and inhibits glycogenolysis. However, in the insulin deficient or insulin resistant patient, glycogen stores are depleted and replaced with stores of ketone bodies (see below).

In the intracellular process of storage of amino acids in muscle as protein, insulin stimulates the production of amino acids and their incorporation into protein. In the absence of insulin, the amino acids stored in the muscle or other tissues, protein manufacture is reduced, and all available amino acids are metabolized to pyruvate, oxaloacetate, and β -ketoglutarate. The pyruvate can be converted to acetyl-CoA which can be further metabolized to acetoacetate. free fatty acid-CoA, or enter the cholesterol synthetic pathway via HMG CoA. In this case, there is production of ketones, fatty acids, and cholesterol.

In the intracellular process of storage of metabolic fuel within the adipose tissue, insulin stimulates lipoprotein lipase. Lipoprotein lipase is synthesized primarily in fat and muscle, and when secreted into the extracellular space, the enzyme is associated with the surface of endothelial cells. Lipoprotein lipase hydrolyzes free fatty acids from triglyceride-rich lipoproteins (i.e. chylomicrons, very low density lipoproteins). Free fatty acids liberated from the lipoproteins are then taken up by adipose tissue, esterified into triglycerides for storage in fat droplets or adipocytes. Insulin stimulates the synthesis and secretion of lipoprotein lipase, inhibits lipolysis of triglycerides stored in adipose tissue, and promotes glucose uptake into the fat stores to provide a glycerol substrate within the adipocytes for esterification of the fatty acids.

In cases whereby there is limited insulin supply or responsivity, there is an enhanced production of free fatty acids. The excess of free fatty acids stimulates the production of ketones (β -hydroxybutyrate, acetoacetate) and the release of ATP. Diabetic ketoacidosis (DKA) describes a clinical situation whereby there is a severe elevation of ketones in the tissues and peripheral circulation with concomitant hyperglycemia. In hepatocytes, mitochondria produce ketone bodies, which form as the result of β -oxidation of fatty acids. Glucagon further stimulates the hepatic ketogenic state; glucagon lowers malonyl coenzyme A levels (the first enzymatic step in the production of fatty acids) which in turn stimulates the activity of carnitine acyltransferase I, an enzyme that translocates fatty acids from cytosolic to intramitochondrial spaces. The fatty acids once in the mitochondria are converted in the absence of glucose to ketones.

The production of excess ketones in DKA is uncontrolled: normally insulin stimulates the ketoacid tissue uptake and the high concentration of ketones themselves saturates tissue uptake. However, in DKA, the only resultant mechanism to remove or excrete excess ketones is via the kidneys. Hyperketonuria causes osmotic diuresis, which in turn causes intravascular volume depletion and dehydration, leading to urinary electrolyte loss. The hyperosmolarity exaggerates the intracellular dehydration.

The hallmark of NIDDM is peripheral tissue insulin resistance. The characteristic post-insulin receptor defect has been difficult to target therapeutically, however, there are working hypotheses to be exploited during drug development. One theory to explain how insulin resistance comes about is the single gateway theory. In the liver, it is thought that insulin is acting not directly on the hepatocytes, but through an indirect means. In this theory, insulin resistant fat cells over produce free fatty acids. It is the free fatty acids that circulate to the liver,

muscle, and others tissues to mediate insulin resistance by a yet unknown mechanism of action.

Another explanation of insulin resistance is free fatty acid response within adipose tissue. In this theory, free fatty acids stimulate the adipocyte production of TNF α and TNF α creates insulin resistance locally and distally within other peripheral tissues. It is thought that TNF α mediates insulin resistance within adipose tissues by stimulating de-differentiation by inhibiting peroxisome proliferator receptor- γ (PPR- γ) and CAAT-enhancer binding protein α (CEBP α) while activating serine-threonine phosphorylation via the MAP kinase cascade. TNF α has been shown to stimulate lipolysis. Further, TNF α stimulates apoptotic signals by activating capases. Within the skeletal muscle TNF α inhibits insulin stimulated glucose uptake, and directly affects the insulin signaling pathway; it stimulates phosphorylation of the IRS-1; and inhibits PPR- γ and CEBP α . An example of the importance of TNF α on the mediation of insulin resistance are recent studies in adipocyte macrophages whereby it has been shown that TNF α has a direct effect on macrophages metabolism (a shift from glucose utilization to free fatty acid production) and a direct effect on PPR- γ and CEBP α .

Type II DM is associated with metabolic syndrome X, also referred to as insulin resistance syndrome, or metabolic syndrome. This syndrome is characterized by hypertriglyceridemia, low serum high density lipoprotein (HDL) and cholesterol, hypertension, central obesity, defective fibrinolysis, and arteriosclerosis. Syndrome X, "the deadly quartet" of obesity, NIDDM, hypertension, and dyslipidemia are common metabolic disorders that have been shown to predispose the patient to early cardiovascular disease, including but not limited to coronary artery disease, heart failure, or congestive heart failure. In these cases, the pancreatic β -cells produce insulin, but the peripheral tissues are physiologically unresponsive to insulin. Thus, the mechanisms of insulin deficiency are active and the resultant hyperglycemia, hyperlipidemia, and others described are present. Clinically, the patient exhibits the signs and symptoms of NIDDM, and unfortunately few therapeutic alternatives are available. Table 50 lists the current candidate therapeutic interventions that are in development for the treatment of IDDM and NIDDM.

Metabolic Syndrome X- It is well known that individuals who are diagnosed with metabolic syndrome X progress to a diagnosis of IDDM. One explanation of the transition of insulin independent to insulin dependent DM is that the overactive, uncontrolled pancreatic β -cells in NIDDM may generate oxygen free radicals that are deleterious to the β -cells and they undergo apoptosis. Another theory that may explain the loss of β -cells is that free fatty acids produced in adipose, hepatic, and

other tissues may compromise the activity of the functioning pancreatic β -cells and ultimately leads to β -cell apoptosis and death. Lastly, the overexpression of TNF α within adipose tissue may activate apoptotic signals within the pancreatic β -cells.

Therefore, in cases of NIDDM, it is clinically advantageous to blunt the progression of the disease to syndrome X. Therapeutic alternatives to treat NIDDM are as follows: 1) diet modifications that are aimed at lowering the daily intake of glucose (carbohydrates) and lipids; 2) low doses of exogenous insulin can be used to inhibit the patient's production and secretion of insulin from the pancreatic β -cells; 3) oral hypoglycemic agents, e.g. sulfonylureas (first and second generations), biguanides, thiazolidinediones, and α -glucosidase inhibitors. Once in syndrome X, there are many other therapeutic alternatives that are added to the regimen to treat the "deadly quartet" as described above.

Novel therapeutic alternatives are required to be developed to meet the need of the population of NIDDM as well as those individuals in which progression to syndrome X has occurred. Table 56 lists the current candidate therapeutic interventions in development for the treatment of one or more of the deadly quartet that is part of metabolic syndrome X.

Many human primary and metastatic tumors express critical proteins required for the maintenance of growth and dedifferentiation along with proteins that may inhibit growth or enhance terminal differentiation. For example, breast adenocarcinomas express at significant levels peroxisome proliferator activated receptor gamma (PPAR γ), that when activated by a specific ligand, will induce terminal differentiation of malignant breast epithelial cells. Although, specific activators of PPAR γ have been developed for the treatment of NIDDM, the antiproliferative and terminal differentiation effect may be exploited for the development of anti-neoplastic agents. Further, agents affecting the PPAR γ pathway may be desirable candidate therapeutic interventions for cancer and DM. Current candidate therapeutic interventions for the treatment of cancer are listed in Table 24.

Besides metabolic syndrome X, there are other chronic late complications of IDDM and NIDDM including retinopathy (proliferative and nonproliferative), nephropathy, neuropathy (including symmetric distal polyneuropathy, asymmetric neuropathy, cranial mononeuropathy and mononeuropathy multiplex), peripheral mononeuropathy and, neuromuscular syndromes and autonomic neuropathy, cardiovascular disease, and skin ulcers due to vascular disease. In cases with loss of sensation in the extremities, there is a predisposition to repeated and undetected trauma. Diabetics are also at increased risk for cardiovascular disease. These complications are only partially reduced by achieving tight control of blood glucose levels.

B. Diabetes Insipidus

The polyuric syndrome in which there is a dysfunction in the antidiuretic hormone (ADH, often referred to as vasopressin (AVP)) signalling pathway, with an loss of ADH activity, and is termed diabetes insipidus (DI). Since ADH is responsible for the appropriate concentration and water conservation in the body, clinical manifestations of this disorder include: polyuria, near-continuous thirst, nocturia, hypertonic encephalopathy, circulatory collapse, and hypernatremia. These symptoms can lead to life-threatening syndromes.

In DI, there is a vasopressinergic deficiency or the target organs are unresponsive to ADH (nephrogenic diabetes insipidus). The etiology of the disorder includes disease processes of the supraoptic nuclei, paraventricular nuclei, the hypothalamohypophysial tract, or the pituitary gland. Although 30% of the cases are attributed to neoplastic lesions of the hypothalamus, 30% are post-traumatic, and 30% are idiopathic, with the remaining 10% being attributed to vascular lesions, infections, systemic diseases such as sarcoidosis that affect the hypothalamic function, and mutations in the ADH gene preprohormone processing pathway.

Treatment of DI depends on the level and extent of the vasopressinergic deficiency. In cases, restoration of fluid balance and control of dehydration is paramount. In some cases of partial loss of ADH, relief of symptoms can be attained through the use of vasopressinergic agonists, candidate therapeutic interventions that enhance vasopressin secretion (e.g. clofibrate), or agents that increase the renal response to vasopressin (e.g. chlorpropamide).

In cases of nephrogenic DI, there is an inability of the renal cells to respond to vasopressin. In one form of this condition, there is congenital defects of the vasopressinergic receptor V2, preventing the ADH stimulation of adenylate cyclase and is an X-linked autosomal dominant genetic condition. In another form of nephrogenic DI, there are mutations in the autosomal gene for aquaporin-2 which produce a nonfunctional versions of this water channel.

Although DI is more common, hypersecretion or over-activity of the ADH pathway leads to a syndrome termed inappropriate hypersecretion of ADH (SIADH). In this syndrome there is profound hyponatremia. This syndrome can occur in patients with cerebral disease (cerebral salt wasting) or pulmonary disease (pulmonary salt wasting), in some cases whereby a tumor is hypersecreting vasopressin, or in the absence of complicating disease. In these cases, patients with inappropriate hypersecretion or vasopressin can be successfully treated with agents or candidate therapeutic interventions that interrupt the vasopressinergic signal, for example, meclocycline, an antibiotic that reduces the renal response to vasopressin.

C. Obesity

According to a commonly accepted definition, obesity refers to a condition by which more than 20% or 25% of body weight is due to fat in men and women, respectively. Another, more reliable, index of fat distribution is the body mass index (BMI) which is calculated as the body weight divided by the square of the height (normal range being 20-25 kg/m²). Obesity is a serious illness that can lead to many complications including hypertension, diabetes, cancer, degenerative arthritis, elevated cholesterol, gallstones or inhibited bile secretion, heart attacks and other cardiovascular disease, strokes, sleep disorders, and psychiatric illnesses including anxiety and depression. There is a strong genetic component to obesity, as well as strong correlations between obesity and socioeconomic status.

Tables 5 and 10 lists the possible genes and gene pathways involved in the manifestation of obesity. Specifically, there are two gene pathways that may be associated with a genetic predisposition to obesity, they are leptin and its receptor, and peroxisome-proliferator-activated receptor γ 2 (PPAR γ 2). In the first, the lipostatic hypothesis of obesity achieved prominence for a potential mechanism of inordinate eating. It was determined in mice lacking a specific gene, the *ob* gene, did not become sated after eating and ultimately became obese and diabetic. The product of this gene is a 167 amino acid protein called leptin. Leptin acts as a hormone to reduce food intake and increase energy consumption. The leptin receptor is encoded by the *db* gene. Mice lacking the *db* gene are also obese, but have high levels of circulating leptin. The leptin receptor is found in two forms, the short and long form which are the result of alternative splicing. The long form is found in the hypothalamus.

The mechanism of leptin and leptin receptor dysfunction creating obesity is thought to occur by (i) interfering with the transport of leptin into the ENDOCRINE AND METABOLIC, (ii) impairing leptin receptor signal transduction, (iii) impairing downstream mediators of leptin action, or (iv) causing obesity by a leptin-independent mechanism – for example a mechanism that originates downstream of leptin or that bypasses leptin. Each of these hypotheses invokes a set of candidate genes (with considerable overlap) and implies up or down variation in allele function.

The genes with potential affect on leptin and leptin associated activity are leptin receptor (OB-R), melanocortin 4-receptor (MC4-R), pro-opiomelanocortin (POMC; the precursor of α -melanocyte stimulating hormone), and prohormone convertase 1 (PC1). Two lines of evidence suggest that variation in these genes may affect leptin resistance. First, each gene has been strongly implicated in the leptin

signaling pathway by *in vitro* data. Specifically, PC1 participates in the processing of the prohormone POMC to the α -melanocyte stimulating hormone (α -MSH), which signals decreased food intake in response to leptin. This signal is transmitted through MC4-R, the receptor for α -MSH. Second, mutations in each of these genes have been associated with obesity in humans and, except PC1, in rodents as well. Leptin signaling could be affected by polymorphisms that affect protein levels or function. Furthermore, there may be polymorphisms in the promoters of all four genes as well as the genomic locus of the leptin receptor and three genes implicated in the signal transduction pathway immediately downstream of the leptin receptor.

Other genes involved in the leptin signal include Neuropeptide Y. Each gene in this set has the potential to modulate the biological function of leptin. Neuropeptide Y, which stimulates food intake through the Y1 and Y5 receptors (and possibly others), is inhibited by leptin. Agouti-related protein inhibits MC4-R signaling and is also down-regulated by leptin. Like NPY, the melanin-concentrating hormone has been shown to stimulate feeding. These genes differ from those above in that mutations have not been associated with obesity in humans (although mutations in the neuropeptide Y1 receptor and the agouti-related protein have been associated with obesity in rodents). With the exception of neuropeptide Y (NPY), where the coding region (but not genomic or promoter sequence) has been screened for polymorphism, these genes have not been studied extensively for variation in humans.

In the second gene pathway associated with obesity, PPAR- γ 2, is a transcription factor (described above and in Example 1) and has been demonstrated to be a key regulator of adipocyte differentiation and energy storage. PPAR- γ 2 is involved in the direction of differentiation of preadipocytes to adipocytes. In *in vitro* studies, over expression of PPAR- γ 2 leads the fibroblast cells to differentiate to adipocytes. Furthermore, phosphorylation of PPAR- γ 2 at a serine residue at position 114 reduces differentiation process mediated by PPAR- γ 2. This serine is contained within a mitogen activated protein kinase or related kinase, indicating an intracellular mechanism for the regulated control of adipocyte differentiation. In a recent study, it was determined that 4 of 121 obese subjects were identified as harboring a substitution of proline to a glutamine at amino acid position 115 as compared to none of the normal subjects having the substitution (Ristow et al, NEJM 339(14):953-959). Since the amino acid at position 115 is near to the serine phosphorylation site at 114, it is suggestive that such a substitution can be predisposing to aberrant PPAR- γ 2 activity.

Other genes that be involved in the genetic differences in obese versus normal weight subjects include signaling genes based on two observations. First,

although no human or rodent models are available to assess the affect of mutation on body mass, it has been shown that JAK2 and STAT3 knockouts are embryonic lethals. This would seem to indicate functions beyond regulation of body mass. Second, there is considerable redundancy in most signal transduction pathways, and there may be compensatory mechanisms to overcome any effects of polymorphism in JAK2 or STAT.

As depicted in Table 51, there are many new candidate therapeutic interventions in development. The targets include galanin, β 3-adrenergic receptor, neuropeptide Y, corticotropin releasing factor, and the cholecystokinin receptors.

D. Contraception

The most widely used oral contraceptives are estrogens and progestins alone or in combination. These agents are taken by women each day to prevent ovulation. The combination therapies are either mono-, bi-, or triphasic which are named as such to indicate the level of estrogen in each of the tablets, i.e. monophasic has the same amount, biphasic has two different doses, and triphasic has three. Progestins are delivered in the same tablet, and the ratio of estrogen to progestin allows for a reduction in the overall amount of steroids delivered to the subject as well as more closely approximates the natural steroid ratio during a menstrual period. The phase delivery of steroids to women wishing to block ovulation has limited the untoward side-effects progestins have on the cardiovascular system.

Unfortunately, although very effective, oral contraceptives are associated with undesirable side effects and toxicity. These effects falls into three categories: cardiovascular effects, cancer, and metabolic and endocrinologic effects.

Cardiovascular effects seen in response to oral contraceptives include estrogen increasing serum HDL while lowering serum LDL and progestins decreasing HDL and increasing LDL. This inordinate and unregulated change in the liporpotien balance in women can lead to hypertension.

Estrogen is a growth promoting hormone, and the estrogen found in almost all of the oral contraceptives has been studied for effects on or risk of ovarian, cervical, endometiral, and breast cancer as well as hepatocellular adenoma in women. However, studies have not conclusively demonstrated an association of higher rates of these types of cancers in women that have used oral contraception.

The metabolic and endocrine effects of oral contraceptives are increased fasting glucose levels, peripheral insulin resistance, higher incidence of gall bladder disease, and estrogen mediated increases of hepatic synthesis of serum proteins.

There are other side effects and disease risk that are associated with oral contraceptives that include increased risk of thromboembolism, nausea, vomiting,

dizziness, headaches, decreased libido, visual disturbances, depression, and post-pill amenorrhea. However, there are beneficial effects of oral contraceptives that include reduction of pelvic inflammatory disease, lower incidence of iron deficient anemia, symptomatic relief of endometriosis, improvement of acne and
5 dysmenorrhea, as well as decreased risk to develop ectopic pregnancies, uterine fibroids, and ovarian cysts.

Oral steroid contraceptives also interact with several other drugs and such interactions can lead to loss of efficacy and include altered drug absorption or metabolism. Any agent or compound that induces hepatic microsomal enzymes or
10 reduces the absorption can alter the effectiveness of the oral contraceptives and these include certain antibiotics, anticonvulsants, or antacids. Furthermore, agents that oppose the therapeutic effects of the oral contraceptives include anticoagulants, antidiabetics, and certain antihypertensives (guanethidine, and α -methyldopa).

There are other genes that one may correlate to candidate therapeutic
15 responses or safety and these include: blockade of implantation, blockade of sperm penetration into the egg, or blockade of sperm production.

As depicted in Table 52, there are many candidate therapeutic interventions that are currently in development to be of therapeutic benefit in contraception.

20 *E. Infertility*

Infertility is the involuntary inability to conceive a child. Infertility is the result of one or more of the following functions for the male or female including 1) adequate production of normal motile sperm, 2) ejaculation of sperm through a patent ductal system, 3) the sperm must be able to traverse an unobstructed female
25 reproductive tract, 4) the female must ovulate and release the ovum, 5) the sperm must be able to enter the ovum, 6) the fertilized ovum must be capable of developing and implanting in the appropriately prepared endometrium. Nearly 40% of the infertility cases, the male has a dysfunction or inadequate function.

Couples experiencing infertility have alternatives to alter their reproductive
30 capacity. Although many of the methods are mechanical and require a procedure, such as *in vitro* fertilization and sperm collection and concentration, there are agents that help a female to ovulate, such as antiestrogens and gonadotropins.

F. Hormonal insufficiency related to aging

35 As individuals age, their androgen and estrogen levels decrease. In some cases, estrogen and androgen replacement therapy has been useful to replenish the deficiency and restore the steroid hormone stasis. In these cases, the deficiency may be the result of a loss of the receptor affinity for the ligand, loss of the receptor

levels, reduction in the production of the steroids, or increased metabolic rates of these steroids. As the aging process continues, there may be a natural reduction in the function within the estrogen or androgen target tissues.

5 *G. Osteoporosis*

The condition in which there is bone matrix and mineral loss is termed osteoporosis. The loss of both of these components in bone results in the reduction of strength, and increased incidence of fractures and is characterized by a net excess loss of bone resorption over bone formation. Although there are multiple causes, the most common is involutional osteoporosis which is associated with advancing age and menopause. Osteoporosis can also occur as a result of long periods of immobilization, space flight, parathyroid hormone and vitamin D deficiency, as well as in patients with excess glucocorticoids (Cushing's syndrome, or administration of glucocorticoids for the therapy of autoimmune disease, transplantation, inflammatory diseases, arthritis, asthma, Crohn's disease, atherosclerosis, or infections with potent inflammatory responses such as hepatitis).

In osteoporosis accelerated normal bone loss can be reversed by estrogens. Estrogens inhibit the secretion of IL-1, IL-6, and TNF α . These cytokines enhance the production of osteoclasts, and in addition, estrogen inhibits the production of TGF- β which is thought to mediate the apoptotic signal within osteoclasts. Although estrogen can reverse bone loss in patients with osteoporosis, the doses of estrogen required are associated with higher risk of myocardial infarctions, stroke, breast and endometrial cancers. However, as described above (under *Contraception*), estrogen in lower doses and given with progestins can be of therapeutic benefit for osteoporosis and have a reduced toxicity profile.

Table 53 lists the current candidate therapeutic interventions that are in development for osteoporosis.

H. Acne

The most common form of noninfectious pustular skin disease is acne. It is an inflammatory skin condition affecting the pilosebaceous units and therefore is predominantly found on the face and upper trunk. Several factors can play a role in the progression of acne including 1) androgenic stimulation of the sebaceous glands, and 2) abnormal keratinization and impaction in the pilosebaceous canals causing obstruction of the sebum flow, and 3) proliferation of anaerobic bacteria. Aggravating factors such as oil-based cosmetics, and certain drugs (androgenic hormones, antiepileptics, progestins (as in oral contraceptives), systemic corticosteroids, and iodide and bromide containing agents. There are also endocrine

conditions whereby there is a hypersecretion of androgen, e.g. polycystic ovarian disease, ovarian tumors, or enzymatic hyperactivity for the production of androgens or reduced metabolism of androgens.

Treatment of acne is aimed at one or more of these three causes: topical agents that remove the comedones such as benzoyl peroxide, topical vitamin A preparations enhancing flow of sebum to the surface, and oral 13-*cis*-retinoic acid can decrease sebaceous gland secretion and gland size. Oral vitamin A preparations are known teratogens and should be avoided in patients who are or plan to become pregnant.

Table 54 lists some current candidate therapeutic interventions in development for the treatment of acne and related skin disorders.

I. Alopecia

Under normal conditions, scalp hair grows between 10-15mm each month. Under normal conditions, 80-85% of hair follicles are in the growing anagen stage, and 15-20% are in the dormant or telogen stage. There are multiple factors that affect the transition of the active to dormant stages and vice versa as well as factors that can affect the rate of growth and condition of hair, including physical, chemical, and emotional events. If severe conditions exist, hair growth can completely stop leading to local or wide spread hair loss. There are two types of hair loss, nonscarring (reversible) and scarring (irreversible).

Nonscarring or localized hair loss includes alopecia areata, tinea capitis, trichotillomania, androgenic alopecia, or traction alopecia. Localized hair loss is characterized by well-circumscribed, round, or oval patches of nonscarring hair loss which usually occurs on the scalp, eyelashes, or eyebrows. Patterns and location of hair loss can define whether there is a poor prognosis for return of hair growth.

Alopecia areata may be autoimmune disease and is associated with cases of Hashimoto's thyroiditis, and pernicious anemia; alopecia areata is treated with glucocorticoid topical preparations. Tinea capitis is an infection predominantly with *Trichophyton tonsurans* and is treated with griseofulvin. Trichotillomania is a disorder referring to traumatic, self-induced alopecia and usually results from persistent twisting, rubbing and pulling resulting in localized hair loss and is treated with emotional or psychiatric therapy. Androgenic alopecia is the familiar male pattern baldness that occurs slowly as a thinning of the hair shafts and eventual loss. Androgenic alopecia is genetically predetermined and is dependent on androgens. Traction alopecia occurs in subjects that over use or abuse hair styling, curling, or other traumatic devices or procedures that damage hair to the extent of hair loss. Hair loss can be further associated with secondary syphilis.

Diffuse or generalized hair loss can occur as a result of a disruption of the normal hair growth cycle. In these cases, full loss of scalp hair may be caused by severe psychological or emotional stress, systemic illness, major surgery with general anesthesia, amphetamines, β -blockers, lithium, probenecid, pregnancy, or discontinuation of oral contraceptives. Disruption of the anagen phase via one or more of these hair growth toxicities may weaken the hair shaft and hair breaks easily. For example, cytotoxic cancer chemotherapeutic agents and radiotherapy to the scalp affect the anagen hair growth phase. Retinoids and hypervitaminosis interferes with the keratinization of the the hair shaft. Diffuse hair loss may occur in cases of hyperthyroidism and nutritional deficiency.

Seborrheic dermatitis appears as erythema and yellow greasy scales throughout the scalp may be associated with mild diffuse hair loss.

Lastly, scarring alopecia may be the result of systemic lupu erythmatosus, discoid lupus erythmatosus, morphea, and aplasia cutis.

In all cases of alopecia, removal or cessation of trauma, agents or procedures that are damaging to the hair follicles or shafts is the first line of therapy. Further, glucocorticoids topical agents can be used to reduce inflammatory or autoimmune components of the localized or diffuse hair loss. Topical Minoxidil, for the treatment of male pattern baldness, has shown to effective in only 30% of the cases.

The androgen receptor is encoded by a gene that is known to have a region of polyglutamine repeats (encoded by CAG repeats) in the amino terminal that is responsible for transcriptional activation. In humans, the number of these CAG repeats is polymorphic. Since androgens can be important in acne, hirsutism, and androgenetic alopecia (AGA), a recent study set out to determine whether these polymorphic repeats were associated with the signs and symptoms of these clinical disorders (Sawaya and Shalita, J Cutan Med Surg 3(1):9-15, 1998). The investigators found that normal subjects had a mean of 22 ± 4 ($n=48$) and 21 ± 3 . ($n=60$) CAG repeats in this region of their androgen receptor for men and women, respectively. In contrast, men with AGA had 19 ± 3 and women with AGA had 17 ± 3 CAG repeats. These data are suggestive that CAG repeat length found in a physiologic relevant site in the androgen receptor may be indicative of the role androgens play bin the mediation of adrogenentic alopecia.

Table 55 lists the current agents, drugs, or candidate therapeutic interventions that are in development of the therapy of alopecia.

J. Adrenal dysfunction

The major function of the adrenal cortex is to produce glucocorticoids (cortisol) and mineralocorticoids (aldosterone). Either an excess or deficiency in

adrenal cortical hormones can have major physiologic effects. Cortisol is responsible for the regulation of carbohydrate metabolism, intermediate metabolism, hemodynamic functions, and developmental processes. Excess cortisol is termed Cushing's disease and cortisol deficiency is termed Addison's disease. Aldosterone is a hormone primarily involved in the regulation sodium, potassium, and hydrogen ion balance and secondarily in the regulation of blood pressure. Hyperaldosteronism or hypoaldosteronism are the terms for excess or deficiency of aldosterone. Besides cortisol and aldosterone, there are many other steroids produced in the adrenal cortex; in females the adrenal cortex is the major source of androgens.

The biosynthetic steps for the production of steroids compounds in the adrenal cortex proceeds via a series of enzymatic steps, the first molecule to enter the cycle is cholesterol, intermediates steroids (including DHEA sulfate, 17 α -OH-progesterone, 11-deoxycortisone, testosterone, androstenediones, deoxycortisols, corticosterones), and final products estradiol-17 β (E₂), estrone (E₁), cortisol, and aldosterone. Under normal condtions, cortisol is the major end-product with aldosterone next, and very little estradiol or estrone.

Adrenal cortical steroids are secreted in repsonse to adrenocorticotropic hormone that is secreted from the pituitary in response to stimulation by corticotropin releasing hormone secreted by the hypothalamus. There is a negative feed back loop, in that cortisol inhibits the secretion of ACTH and CRH at the pituitary and the hypothalamus, as well as somatostatin acting in the same manner as cortisol to attnetuate secretion of the hypothalamus and pituitary hormones.

Once secreted, cortisol is approximately 90-93% bound by plasma proteins; albumin and the major protein being corticosteroid binding protein (CBG, transcortin). CBG has a high affinity for cortisol and is not required for transport, nor cortisol function. CBG is produced in the liver and the concentrations found in plasma is genetically determined and is regulated by hormone levels. CBG levels are increased during certain physiological conditions including pregnancy, hyperthyroidism, diabetes, in excess estrogen, and during the administration of oral contraceptives. CBG levels can be low or deficient during periods of malnutrition, in liver disease, multiple myeloma, obesity, hypothyroidism, and part of the nephrotic syndrome. In cases whereby there is an increase or decrease in the levels of CBG, bound cortisol levels increase or decrease, respectively, however there is a constant level of free cortisol. Mineralocorticoids, once secreted, are approximately 60% bound to plasma albumin.

Nearly 99% of the adrenal cortical steroids are metabolized prior to excretion. Thus, any defect or dysfunction in the enzymes involved or in the metabolic rates can result in elevated levels of cortisol or active metabolites.

Further, metabolic enzymatic reactions occur to ensure that products are sufficiently different to not elicit a biological effect in the metabolizing organ. For example, the 11 β -hydroxyl group of cortisol can be metabolized in the liver to the ketone form which is devoid of cortisol receptor binding activity. Conversely, cortisol in the kidney can be metabolized to cortisone which prevents cortisol from binding to the mineralocorticoid receptor in the kidney. Cortisol and aldosterone are cleared from the plasma with a half-lives of 80-120 minutes and 15 minutes, respectively. The changes of metabolic rates can occur via 1) inhibitory influences of plasma binding on clearance rates. 2) enhanced metabolic enzymatic activity. The metabolism of these steroid hormones can be altered by: 1) decreased metabolism, or 2) increased metabolism. Glycyrrhetic acid, present in licorice, and carbenoxolone block the 11 β -hydroxysteroid dehydrogenase activity and thereby prevent the conversion of cortisol to cortisone. Thus alterations as described above can lead to enhanced or decreased adrenal cortical steroid hormone activity and physiologic response.

Nearly 80% of the primary adrenocortical insufficiency cases are due to autoimmune destruction of the adrenal cortical tissue. Autoimmune adrenocortical insufficiency has some genetic predisposition; 40% of the cases have first or second degree relatives with similar clinical patterns. Nearly all the cases of secondary adrenocortical insufficiency is the result of limited secretion of ACTH.

Therapy of adrenocortical insufficiency is treated in the acute setting with intravenous soluble steroids and control of fluid and electrolyte balance. For the maintenance of cortisol levels, these patients are put on a schedule of cortisol administrations that mimic the normal physiologic circadian rhythm.

Hypersecretion of cortisol is termed Cushing's syndrome may be caused by adenocortical tumors hypersecreting cortisol, conditions that increase ACTH secretion, and by prolonged administration of corticosteroids. This syndrome is characterized by a moon face, increased fat pads, red cheeks, protuberant abdomen, abdominal striae, poor muscle development, poor wound healing, and bruisability with ecchymoses. Therapy of Cushing's syndrome is dependent on the etiology of the disease. Adrenocortical and pituitary tumors can be surgically removed, however in each case disruption of normal glandular function must be avoided. Bilateral removal of adrenal glands can lead to Nelson's syndrome which is thought to arise due to the loss of cortisol negative feedback on the pituitary gland. In the absence of tumors, drugs may be used to limit the secretion of ACTH or cortisol

they include: reserpine, bromocriptine, cyproheptadine, and valproate sodium can be used to reduce the secretion of ACTH, however only a minority of patients respond. Ketoconazole inhibits cortisol secretion.

Cortisol and the many synthetic congeners are the mainstay drug or therapy for many inflammatory diseases, conditions, or disorders and in the transplantation setting. Corticosteroids affect the immune response by decreasing growth and development of mast cells, inducing apoptosis, suppressing lymphocyte generation of IL-5 and other cytokines, inhibiting some mediator release, inhibiting cytokine production, inhibiting the transcription of cytokines (for example IL-8, TNF- α , prototypic antiviral chemokine (regulated-on-activation normal T-expressed and secreted, RANTES), and GM-CSF), and inhibiting nitric oxide synthesis. As well as providing antiinflammatory therapy, corticosteroids suppress immune function by inhibiting the activation of T cells. Steroids are highly effective in the early induction and maintenance regimens and are first line therapy in acute allograft rejection.

Glucocorticoid associated side effects include increased appetite, weight gain, fluid retention, acne, ecchymosis, development of cushoid facies, hypertension, hyperkalemia, diabetes, hyperglycemia, hyperosmolar state, hyperlipidemia, hepatic steatosis, atherosclerosis, myopathy, aseptic necrosis, osteoporosis, ulcers, pancreatitis, pseudotumor cerebri, psychosis, glaucoma, cataract formation, vascular necrosis, increased susceptibility to infection, impairment of the hypothalamus-pituitary axis, decreased thyroid hormone serum binding proteins, and impaired wound healing.

Mineralocorticoid hypersecretion occurs due to adrenocortical adenoma, bilateral adrenocortical hyperplasia, and adrenal carcinoma. Clinically, the symptoms include hypertension, suppression of plasma renin, hypokalemia and associated disorders or syndromes related to each of these dysfunctions. Therapy for these conditions usually entails uni- or bilateral surgical removal of the adrenal adenoma or hyperplasia. In these cases, cortisol maintenance therapy is initiated as described above.

Mineralocorticoid hyposecretion is treated with supplemental mineralocorticoid therapy.

K. *Thyroid dysfunction*

The thyroid gland secretes thyroxine (3, 5, 3', 5'-tetraiodothyronine, T₄) and 3, 5, 3'-triiodothyronine (T₃). The principal role for these two hormones is to regulate tissue metabolism and, in infants and young children, to regulate growth, development, and maturation of the nervous system and bone and joints. The

enzymatic pathway for the generation of T_4 and T_3 as well as the conversion of T_4 to T_3 (within the liver and the kidneys) are known and genes involved in these pathways are listed in Table 5.

The regulation of thyroid hormone secretion is part of the hypothalamus-pituitary axis; by which thyroid releasing hormone (TRH, secreted from the hypothalamus) acts on the pituitary gland to secrete thyroid-stimulating hormone (TSH) that acts on the thyroid gland to stimulate the secretion of T_4 and T_3 . Somatostatin, and other neuropeptides or neurotransmitters regulate the thyroid gland secretion activity by inhibiting secretion of TSH at the level of the pituitary gland. T_3 can directly suppress the the level of proTRH mRNA in the paraventricular nucleus of the hypothalamus.

Circulating thyroid hormones are bound to throxine-binding globulin, transthyretin, or albumin, which are involved in the transport of the thyroid hormones to their target tissues. The concentrations of these binding proteins change under various physiologic conditions and can affect the efficacy and tissue distribution of the thyroid hormones. These condiditions include 1) increased serum thyroid hormone binding proteins: pregnancy, exposure to supraphysiologic levels of estrogen, hepatic cirrhosis or acute hepatitis, acute intermittent porphyria, exposure to heroin or methadone, and clofibrate; 2) decreased serum thyroid hormone binding proteins: protein malnutrition, hepatic failure, chronic illness, nephrotic syndromes, exposure to L-asparaginase, congenital abnormality (X-linked) of the binding protein genes, exposure to androgenic steroids of pharmacologic doses of glucocorticoids.

The mechanism of action of T_3 and T_4 on the target tissues is thought to occur via thyroid hormone intracellular receptors that binds the hormone ligand and via a process of entry into the nuclear compartment, the hormone-receptor complex activates DNA transcription genes having a thyroid receptor response element in the promoter region.

Dysfunction of thyroid hormone pathway is clinically expressed as either hyperthyroidism or hypothyroidism. In either case, there are multiple levels of possible or potential disruptions of the thyroid hormone signalling pathway.

Hyperthyroidism or Graves' disease is also termed thyroidtoxicosis and may be associated with catecholamine excess, toxic multinodular goiter, toxic adenoma, iodide-induced hyperthyroidism, subacute thyroiditis, factitious (exogenous) thyrotoxicosis, neonatal thyrotoxicosis (mother with Graves' disease), TSH-secreting pituitary tumors, nontumorigenic pituitary-induced hyperthyroidism, choriocarcinoma or hydatiform mole, struma ovarii, and hyperfunctioning thyroid carcinoma. Clinically, symptoms include marked ophthalmopathy (preorbital

swelling, exophthalmos, limitation of extraocular movements, protruding eyes and easy tearing), pretibial myxedema, tachycardia, elevated systolic blood pressure, and increased inotropic activity in the myocardium.

Therapy of hyperthyroidism follows two stages, 1) reestablishment of the euthyroidism, and 2) induction of a permanent alteration of thyroid function. In the first, reduction of elevated thyroid hormone secretion can be achieved by administration of thiourea derivatives (for example, propylthiouracil, methimazole, carbimazole). These agents inhibit the organification of iodine within the thyroid gland and suppress the production of the thyroid hormones. Side effects of these thiourea compounds include maculopapular rash, hepatocellular damage, agranulocytosis, and vasculitis. Other compounds used for the acute therapy of hyperthyroidism include lithium, iopanoic acid, and iopadate. In the second stage of therapy for hyperthyroidism, long-term therapy of propylthiouracil may induce remission of the hypersecretion. If remission is not attained, surgical removal of the thyroid gland, or treatment with ^{131}I . Unfortunately, radical therapies to remove or ablate function of the thyroid gland can lead to hypothyroidism.

In hypothyroidism, there is impaired secretion of the thyroid hormones. Hypothyroidism may be associated with acquired disease (Hashimoto's thyroiditis, idiopathic myxedema, ^{131}I radiotherapy, external radiation therapy to the neck area, subacute thyroiditis, cystinosis, impaired function of thyroid gland (iodine deficiency or excess, drug induced (lithium carbonate, para-aminosalicylic acid, thiourea drugs, sulfonamides, phenylbutazone, and others)), congenital genetic defects (biosynthetic enzymes for the thyroid hormones, thyroid agenesis, thyroid dysgenesis or ectopy, maternal iodide or antithyroid drugs), hypothalamic dysfunctions (neoplasms, eosinophilic granuloma, therapeutic irradiation), or pituitary dysfunction (neoplasms, pituitary surgery or irradiation, idiopathic hypopituitarism, Sheehan's syndrome, exposure to supraphysiologic levels of dopamine). Clinically, symptoms include weakness, fatigue, lethargy; dry, coarse skin; swelling of the hands, face and extremities; cold intolerance and decreased sweating; modest weight gain; decreased memory; hearing impairment; arthralgia and paresthesias; constipation; and muscle cramps. In infants or young children in which hypothyroidism remains unchecked during the first two years of life, irreversible mental retardation as part of a syndrome called cretinism develops.

Therapy of hypothyroidism includes the replacement of synthetic thyroid hormones, T_4 and T_3 . In these cases, hormone replacement therapy is sufficient to restore euthyroidism. Special cases of hypothyroidism, for example those individuals with angina and hypothyroidism require special monitoring since the replacement hormones may stimulate the myocardial oxygen demands in a

myocardium that can not produce adequate myocardial blood flow. Another special case are patients with severe myxedema coma, and event that may arise in patients with severe hypothyroidism and are subjected to additional physiologic stresses.

Anthithyroid antibodies can be part of an autoimmune thyroid disease, such as Hashimoto's or Graves' disease. Patients may have serum antibodies formed to thyroid peroxidase (common), serum thyroglobulin, or to the TSH receptor.

L. Parathyroid dysfunction

Parathyroid hormone is secreted by the parathyroid glands. The hormone is responsible for the regulation of bone resorption and calcium mobilization. In addition to increasing the the plasma Ca^{+} levels and depressing the plasma phosphate levels, parathyroid hormone increases the excretion of phosphate in the urine.

In cases of pseudohypoparathyroidism, patients have normal circulating levels of parathyroid hormone, but lack the GTP-binding protein to allow hormone receptor-G-protein stimulated adenylate cyclase activity and subsequent increases in intracellular cAMP. In another form of pseudohypoparathyroidism, there is an adequate GTP-binding protein, but there is lacking the intracellular messenger system to allow parathyroid hormone mediated phosphaturic action of the hormone within the target tissues. In cases of parathyroidectomy, hypocalcemia, tetnus, and hyperphosphatemia occurs. Administration of parathyroid hormone can restore calcium and phosphate ion stasis.

In cases of parathyroid hormone excess, usually a result of inordinate administration of parathyroid hormone or a tumor hypersecretion of parathyroid hormone, the symptoms include hypercalcemia, hypophosphatemia, and demineralization of the bones, and the formation of calcium containing kidney stones. Removal of the tumor or adjustment of the parathyroid hormone administration schedule is the prudent course of treatment. Secondary hyperparathyroidism may be the result of chronic renal disease.

In nearly 20% of cancer patients there is marked hypercalcemia as result of bone metastases that produce the hypercalcemia as a result of the eroding bone. The bone erosion may be the result of prostaglandin E and the tumor or cancerous cells. Further some cancers cells hypersecrete 1,25-dihydroxycholecalciferol, or another bone related hormones. In some cancers, there has been detected hypersecretion of parathyroid hormone-related protein. Tumors in this category include breast, kidney, ovary, and skin.

Although the above description includes the hypothalamus-pituitary-target gland axes, there are other organs that have endocrine functions. These include the kidneys, the heart, and the pineal gland.

The kidneys regulate blood pressure via the renin-angiotensin system. The kidneys produce and secrete renin (in the juxtaglomerular apparatus), an acid protease that acts on angiotensinogen to form angiotensin I. The next enzyme in the pathway is angiotensin converting enzyme (ACE, located in the lungs and
5 elsewhere) which converts angiotensin I to angiotensin II. Angiotensin II acts directly on vascular smooth muscle to to arteriolar constriction and leads to an increase in blood pressure, on the adrenal cortex to stimulate secretion of aldosterone, and in the cerebral cortex to decrease the baroreflex potentiation of the pressor effects. Angiotensin II is metabolized by various peptidases
10 (aminopeptidase) and is sequestered in vascular beds of tissues by as yet unknown molecule trapping mechanism.

ACE, angiotensin and renin receptors, and regulation of renin secretion have proven excellent candidate targets for drug intervention for the treatment of hypertension and other cardiovascular disease. Other likely candidates for the
15 therapeutic intervention of the renin-angiotensin system are listed in Table 5 and Table 11.

The kidneys, and to a lesser extent the liver, also produce and secrete erythropoietin. In adults, erythropoietin is produced by the interstitial cells in the peritubular capillary bed of the kidneys and the perivenous hepatocytes in the liver.
20 Erythropoietin regulates the production of erythrocytes by stimulating the number of erythropoietin-sensitive committed stem cells in the bone marrow that are converted to precursors and ultimately to mature erythrocytes. When erythropoietin levels are low, erythroid stem cells show DNA cleavage followed by programmed cell death (apoptosis). Erythropoietin reduces the DNA cleavage and stimulates the
25 cells to survive. When the renal mass is reduced in adults by renal disease or nephrectomy, the resultant reduction in the production of erythropoietin, and the inability of the liver production to compensate for this reduction, leads to marked anemia. Synthetic or recombinant erythropoietin has proven to be therapeutically important to those individuals in end-stage renal disease and other anemic conditions
30 such as cancer, trauma, surgery, and others. Other genes involved in the erythropoietin pathway are listed in Table 5.

The myocardium produces and secretes atrial natriuretic peptide (ANP). ANP produces natriuresis, in part by stimulating an increase in glomerular filtration rate, promotes tubule secretion of sodium, and lowers blood pressure by acting
35 directly on the vascular smooth muscle cells and decreases the responsiveness to pressor substances. In the brain, ANP actions are opposite of those directed by angiotensin II. ANP is metabolized by neutral endopeptidase (inhibited by thiorphan) and has a short half-life.

The other endocrine hormone involved in natruiresis is produced and secreted from the adrenal glands and is termed the Na⁺/K⁺ ATPase inhibiting factor. This factor produces natruireses by inhibiting the Na⁺/K⁺ ATPase and produces an increase in bloo pressure.

5 The pineal gland produces and secretes melatonin. In humans, melatonin is produced and secreted during the dark periods of the day and is maintained at lower concentrations during the daylight hours. Melatonin has been implicated in inducing and maintaining sleep. Melatonin is synthesized from serotonin via two enzymes found in the pineal paremchymal cells. Melatonin is secreted via a neural
10 stimulation to the pineal gland. β -Adrenergic stimulation to the pineal gland results in increased stimulation of the porduction and screretino of melatonin. Metabolism of melatonin occurs via 6-hydorxylation followed by conjugation in the liver and is predominantly excreted in the urine.

Cardiovascular and Renal Disease

15 There are some examples whereby there is no direct evidence that a gene or genes are involved in drug response of a candidate therapeutic intervention. In these cases, however, there is genetic data supporting a role of a variance or variances involved in the etiology, progression, or risk of a cardiovascular or renal disease. These cases, including but excluded to are described below with details of current
20 therapies and potential genetic involvment of variances in drug responses.

A. Anemia

 Anemia is a condition in which the number of red blood cells per cubic mm, the amount of hemoglobin in 100 ml of blood, and the volume of packed red cells
25 per 100 ml of blood are less than normal values. Anemia may be clinically manifested as pallor of the skin and mucus membranes, shortness of breath, palpitations of the heart, soft systolic murmurs, shortness of breath, lethargy, and fatigability or other signs and symptoms. Anemia can be caused by three broad defects 1) bone marrow failure, 2) acute blood loss, and 3) hemolysis, however,
30 anemia may be the result of one or more of these three. Anemia is a common manifestation of many different chronic or acute diseases, toxins, therapeutic drugs, nutritional status, endocrine disorders, congenital conditions, autoimmune conditions, alcohol, drug, or substance abuse, trauma, surgery, or any other condition that affects the function or status of the bone marrow, blood volume, or
35 erythrocytes. When anemia develops, there are compensatory physiological mechanisms that are available to attempt to restore tissue oxygenation including

increases in the erythrocyte glycolytic intermediate 2,3-diphosphoglycerate (2,3-DPG; binds to hemoglobin and decreases the oxygen binding affinity) in erythrocytes, increased peripheral dilation, increased cardiac stroke volume, decrease in blood pressure, or other mechanisms.

5 Anemia may be due to drug toxicities. Aplastic anemia or hematologic blood disorders may also be due to a proliferative defect and related bone marrow failure syndromes.

 Anemia due to bone marrow failure usually results in changes in mean cell volume (MCV) can be categorized as normocytic, microcytic, and macrocytic
10 anemia. Normocytic bone marrow failure can be the result of iron deficiency, chronic disease, renal failure, liver disease, endocrine disorders, aplasia, myelodysplasias, myelofibrosis, hematologic or solid tumors, granulomas, human immunodeficiency virus (HIV) infection, and others. Microcytic bone marrow failure can be the result of iron deficiency, chronic disease, thalassemias, aluminum
15 toxicity, thyrotoxicosis, hereditary sideroblastic conditions and others. Macrocytic bone marrow failure can be the result of megaloblastic conditions (cobalamin and folate deficiencies, and congenital disorders), alcoholism, drugs, liver disease, aplasia, myelodysplasias, myelofibrosis, hematologica or solid tumors, granulomas, human immunodeficiency virus (HIV) infection, hypothyroidism, splenectomy, and
20 others.

 Hemolytic anemia primarily due to the destruction of red cells can be the result of congenital conditions (enzyme deficiency, membrane skeletal protein abnormalities, hemoglobinopathies) or acquired conditions (antibody-induced, mechanical fragmentation, and membrane protein anchoring abnormalities). Acute
25 blood loss occurring in trauma, surgery, or acute or chronic disease can lead to excessive blood loss.

 Drugs or other agents known to cause anemia include cancer chemotherapeutic agents (antimetabolites, alkylating agents, hydroxyurea, cytosine arabinoside and others), anti-inflammatory agents (aspirin, non-steroid anti-
30 inflammatory agents, phenylbutazone, gold compounds), antibiotics (chloramphenicol, penicillin, cephalosporins, sulfonamides and others), anticonvulsants (phenytoin and others), dihydrofolate reductase inhibitors (methotrexate, pyrimethamine, trimethoprim, triamterene, pentamidene, and others), antiviral agents (zidovudine and others), immunosuppressive agents (azathioprim
35 and others), antiarrhythmic agents (procainamide, quinidine and others), antihypertensive agents (alpha-methyldopa), antimalarials (primaquine and others), and the anticoagulants (warfarin and heparin and others).

Therapy of anemia includes blood transfusion, removal of the agent or toxin causing the anemia, or treating the underlying cause of the anemia. In some cases of anemia, erythropoietin can be used to stimulate the erythrocyte precursor cells in the bone marrow cells to produce mature erythrocytes.

5 A gene, genes, or gene pathway involved in the etiology of anemia or associated disorders or potential sites for targeted drug therapy of anemia are depicted in Table 11 with the specific gene list in Table 6. Current candidate therapeutic interventions in development for the treatment of anemia are listed in Table 57.

10 *B. Angina*

Angina pectoris is a common clinical manifestation of coronary artery disease. Angina is a clinical syndrome including chest pain or discomfort brought on by exertional or anxiety, typically lasting several minutes. Patients with angina are at increased risk of myocardial infarction heart failure and death. Angina is a symptom of myocardial ischemia that is the result of myocardial oxygen demand not met by myocardial oxygen supply (for more details see below under *Ischemia*). Although the most common cause of myocardial ischemia is atherosclerotic coronary artery disease, there are other factors that may lead to this clinical syndrome, including thromboembolic disease and vasospasm. Factors related to myocardial oxygen demand include heart rate, contractility, and wall tension (ventricular volume and ventricular pressure). Unstable angina refers to angina of which occurs at rest or without a specific (exertional or environmental) trigger. Stable angina refers to predictable, event-induced chest pain. Unstable angina has been correlated with progression to acute myocardial infarction in 20% of the cases. More than 50% of the patients with unstable angina have multi-vessel disease with eccentric, irregular, or ulcerated atherosclerotic lesions associated with endothelial disruption and adherent thrombus.

Another form of angina is variant angina which is characterized by chest pain accompanied by a transient ST-segment changes (either ST elevation or depression) and ventricular arrhythmias.

Angina can often be controlled by nitrates, β -adrenergic blockers, calcium channel blockers, antiplatelet and antithrombin therapy, or combination thereof.

35 Genes, and gene pathway involved in the etiology of angina and associated disorders or potential sites for targeted drug therapy of angina are depicted in Table 11 with the specific gene list in Table 6. Current candidate therapeutic interventions in development for the treatment of anemia are listed in Table 58.

C. Arrhythmia

Cardiac arrhythmias occur as a result of abnormalities of impulse generation, impulse conduction, and combined abnormalities of impulse generation and conduction. Some cardiac arrhythmias may lead to asymptomatic conditions, others lead to clinical symptoms and may be life-threatening. Abnormalities of impulse generation includes abnormal automaticity (abnormal pacemakers), triggered activity as a result of early or delayed after-depolarizations. In both alterations of automaticity and triggered activity, generation of impulses in fibers that are normally incapable of normal automaticity, e.g. atrial and ventricular tissue, ensues. Within the myocardium the conduction system can become a cardiac pacemaker. For example, the atrioventricular (AV) node.

Abnormalities of impulse conduction occurs via a process called reentry. In reentry, there occurs an area or region that is slow or unable to conduct electrical signals. This defect in conduction permits a wave of excitation to propagate continuously within a closed circuit. In these cases, the surrounding tissue is not at the same pace as the surrounding tissue and the electrical impulse passes through the normal tissue and can spread in a multi-directional manner which leads to marked asynchrony.

Heart block is the condition whereby the conduction from the atria to the ventricles is interrupted. Myocardial disease may decrease or stop conduction in one or more regions. Heart block may be complete, incomplete, include a right- or left bundle branch block, hemiblock or fascicular blocks.

Ectopic foci of excitation occurs when there is myocardial disease that renders the His-Purkinje fibers or other fibers to discharge electrical activity spontaneously. This condition leads to increased automaticity, potentially leading to extrasystole, premature beats, atrial or ventricular or nodal paroxysmal tachycardia, or atrial flutter.

Arrhythmias may also be localized to the atrial or ventricular regions. Atrial arrhythmias include atrial tachycardia, or paroxysmal atrial tachycardia with block, atrial flutter, or atrial fibrillation. Ventricular arrhythmias can include all of the previous described types of arrhythmias but also include paroxysmal ventricular tachyarrhythmia as well and ventricular fibrillation.

Accelerated AV conduction (Wolff-Parkinson-White syndrome) or the Lown-Ganong-Levine syndrome are examples of other arrhythmias that are characterized by specific electrocardiogram abnormalities.

Therapy for arrhythmias includes an understanding of the type, underlying mechanism, and treatment targeted to restore normal cardiac function. However, in some cases, mechanisms can only be inferred and therapy is based on empirical

knowledge. Current antiarrhythmic drugs can be classified as the following broad categories: Na⁺ channel blockers, K⁺ channel blockers, Ca⁺ channel blockers, β -adrenergic blockers, and digitalis. In each of these categories, there is a blockade of the activity of the specific ion channel or receptor mediated activation of the myocardial activity. Digitalis is the exception, having multiple pharmacologic effects including Ca⁺ current inhibition, stimulation of vagal tone to the myocardium, and a reduction in the K⁺ currents within the atrium.

A gene, genes, or gene pathway involved in the etiology of arrhythmia or associated disorders or potential sites for targeted drug therapy of arrhythmia are depicted in Table 11 with the specific gene list in Table 6. Current candidate therapeutic interventions in development for the treatment of arrhythmias are listed in Table 59.

Hypertension

Hypertension is the clinical syndrome in which there is sustained elevation of systemic arterial pressure. There may be conditions of specific arterial hypertension to specific organs, including pulmonary, renal, hepatic arterial hypertension.

Systemic hypertension is a common abnormality that can be the result of a variety of conditions including: adrenocortical disease (Conn's syndrome, aldosteronism, hypersecretion of glucocorticoids, hypersecretion of mineralocorticoids, and pseudohyperaldosteronism), pheochromocytoma, justaglomerular carcinoma, renal hypertension, renal disease (glomerulonephritis, pyelonephritis, polycystic disease, Liddle's syndrome, hypokalemic nephropathy, low-renin hypotension), Narrowing of the aorta, oral contraceptives, neurovascular compression of the rostral ventrolateral medulla. However, in most cases, the etiology is unknown (termed essential hypertension).

Therapy of hypertension includes α - or β -adrenergic blockers, inhibition of the renin-angiotension system, or converting enzyme, and calcium channel blockers. In cases whereby hypertension is the result of a condition, as listed above, the primary condition is treated with ancillary antihypertensive added. Further, reduction in the intake of sodium in the diet has been shown to assist the reduction of systemic arterial pressure.

A gene, genes, or gene pathway involved in the etiology of hypertension or associated disorders or potential sites for targeted drug therapy of hypertension are depicted in Table 11 with the specific gene list in Table 6. Current candidate therapeutic interventions in development for the treatment of hypertension are listed in Table 60.

E. Hypotension

Hypotension is the condition of subnormal blood pressure. Hypotension may be the result of orthostatic hypotension, anemic conditions, fulminant meningococccemia or other infections, blood transfusions, trauma, traumatic brain injury, hepatic or renal failure, and drug induced.

Hypotension is currently treated with methoamine, peripheral sympathomimetics, and vasopressin. A gene, genes, or gene pathway involved in the etiology of hypotension or associated disorders or potential sites for targeted drug therapy of hypotension are depicted in Table 11 with the specific gene list in Table 6. Current candidate therapeutic interventions in development for the treatment of hypotension are listed in Table 61.

F. Ischemia

Myocardial ischemia develops when the metabolic demands exceed oxygen delivery to the myocardium. Factors that influence the myocardial oxygen supply include the oxygen capacity of the blood, coronary blood flow and vascular resistance. Factors that affect myocardial oxygen demand are heart rate, contractility, and systolic wall tension. Any agent or physiologic factor that decreases myocardial oxygen supply or increases myocardial oxygen demand may potentially lead to myocardial ischemia. There are conditions that lead to myocardial ischemia including hypertension, arrhythmias, coronary artery disease, rheumatic fever, congenital heart defects, heart failure, and myocardial infarction.

The identification and extent of myocardial damage due to myocardial oxygen demand and reduced supply clinically manifests as myocardial infarction, sudden death, angina pectoris (either uncomplicated or with infarct), and coronary insufficiency.

Therapies for myocardial ischemia currently available are described within other sections of this invention and can be found under the following sections: thrombosis, angina, hypertension, arrhythmias, and heart failure. A gene, genes, or gene pathway involved in the etiology of ischemia or associated disorders or potential sites for targeted drug therapy of ischemia are depicted in Table 11 with the specific gene list in Table 6. Current candidate therapeutic interventions in development for the treatment of myocardial ischemia are listed in Tables 57, 59, 60, 62, and 64.

G. Heart Failure

Heart failure is a syndrome in ventricular dysfunction if accompanied by reduced exercise capacity. Heart failure is the final condition from a variety of cardiovascular disorders including coronary heart disease, long-standing

hypertension, valve deformities or valvular heart disease, rheumatic heart disease, nutritional cardiac disease and cardiomyopathies. Other diseases or conditions associated with heart failure include infections (systemic or cardiac specific (myocarditis), infiltrative disorders (amyloidosis, hemochromatosis, sarcoidosis), electrolyte disorders, myocardial specific toxins (substances of abuse, cancer chemotherapeutic agents), lupus erythmatosus, rheumatoid arthritis, diabetes mellitus, thyroid disease, hypoparathyroidism, pheochromocytoma, and sustained or prolonged tachycardia.

Ultimately, in the failing heart, inotropic action is compromised and the resultant loss in cardiac output renders the myocardium unable to meet the systemic and peripheral metabolic demands leading to various clinical symptoms including cardiac enlargement, weakness, edema, prolonged circulation time, hepatic enlargement, shortness of breath, sensation of suffocation, and distention of peripheral veins. Dyspnea on exertion is a prominent symptom, leading to paroxysmal, and in severe cases, frank pulmonary edema.

Physiological compensatory mechanisms of heart failure can be broadly described as increased heart rate, increased preload and afterload, and cardiac hypertrophy. Each of these physiological changes are attempts to increase cardiac output which is dependent on heart rate, blood pressure and contractility.

Although the most common form of heart failure is left ventricular failure (70-90%), there are conditions whereby diastolic dysfunction occurs (10-30%). Clinically these two are treated differently. For left ventricular (LV) failure, the current therapies include a combination of antihypertensives (ACE inhibitors), diuretics, and positive inotropic agents. Refractory cases of LV failure, additional diuretics, vasodilators, and β -adrenergic blockers are added to the regimen. In diastolic dysfunction leading to failure Ca^{++} channel blockers are the first line of therapy with ACE inhibitors and β -adrenergic blockers added in refractory cases.

Heart failure is further associated with a variety of co-morbidities that can worsen the condition and prognosis including septicemia, hypo-osmolality, primary thrombocytopenia, renal hypertension disorder, myocardial infarction, pulmonary embolism, arrhythmias, intracerebral or subdural hemorrhage, cerebral thrombosis, hypotension, pneumonia, chronic renal failure, and decubitus ulcers.

A gene, genes, or gene pathway involved in the etiology of heart failure or associated disorders or potential sites for targeted drug therapy of heart failure are depicted in Table 11 with the specific gene list in Table 6. Current candidate therapeutic interventions in development for the treatment of heart failure are listed

in Table 11 and complications associated with heart failure in Tables 59, 60, 62, and 64.

H. Thrombosis

5 Thrombosis is the formation of a blood clot in a blood vessel. If the thrombotic clot is large enough it may occlude the vessel and create tissue hypoxia. If unchecked, thrombosis can be a major medical problem and is associated with vessels that have sluggish blood flow, including in veins of extremities after surgery or delivery, conditions of reduced cardiac output, or in coronary or cerebral arteries
10 where the intima is damaged by atherosclerotic plaques (see below) or damage to the endocardium. Areas of thrombi have a tendency to break off from a vessel wall and can travel to distant sites, termed emboli, and create damage to other organs.

The activation of coagulation occurs via a coordinated process of clotting factors leading to the formation of thrombin which then activates the conversion of
15 fibrinogen to fibrin and clot formation ensues. However, in the endothelial cell, when thrombin binds to thrombomodulin, thrombin has anticoagulant activity by first activating protein C. Activated protein C then inactivates an inhibitor of tissue plasminogen activator and conversion of plasminogen to plasmin occurs. Plasminogen is converted to active plasmin when tissue plasminogen activator
20 hydrolyzes the bond between arg560 and val561. Plasmin is responsible for the enzymatic breakdown of clots.

Atherosclerosis is a complex combination of hyperlipidemia, injury to the endothelium, and inflammation. The interaction of these multiple processes in association with local genetic and hemodynamic influences may promote the
25 formation of atheromatous plaques as a reparative response of the arterial wall. Atherosclerotic plaques are composed of thrombogenic lipid-rich core protected by a fibrous cap comprising smooth muscle cells and inflammatory cells. The inflammatory cells are predominantly macrophages. As atherosclerotic plaques build blood flow is reduced creating ischemia in tissues down stream from the area
30 of the plaque.

In another model, the stenosis created by the plaques may be a part of the resulting ischemic event. Frequently, less obstructive but more vulnerable plaques occur which are characterized by a thinned fibrous cap, marked lipid accumulation, a large number of macrophages, and a smaller amount of smooth muscle cells. It
35 has been proposed that since these plaques are more prone to rupture creating contact with the highly thrombogenic materials of the lipid-rich nucleus of these lesions, thrombosis is stimulated.

Advanced atherosclerotic lesions are caused by a series of cellular and molecular events involving replication of smooth muscle cells and macrophages on the vessel wall. The interaction of these cells with the T lymphocytes can lead to a fibroproliferative response. Large amounts of connective tissue produced by these smooth muscle cells consist of macrophages, T lymphocytes, smooth muscle cells, connective tissue, necrotic residues, and varying amounts of lipids and lipoproteins.

Endothelial cells maintain the vessel surface in a non-thrombogenic state, preventing platelet and leukocyte adhesion, and act in maintaining the vascular tonus by releasing nitric oxide, prostaglandin, and endothelin. These cells also produce growth factors, cytokines, and chemokines to maintain the integrity of the collagen- and proteoglycan-rich basement membrane. Changes in some of these functions may trigger cell interactions with monocytes, platelets, smooth muscle cells, and lymphocytes. Hyperlipidemia and hypercholesterolemia are sufficient to induce dysfunction of the endothelial modulation of the vasoactive reactions and arteriolar tonus.

Anticlotting therapy includes heparin, streptokinase, urokinase-type plasminogen activator, and tissue-plasminogen activator. Coumarin derivatives such as dicumarol and warfarin can also be effective anticoagulants. These compounds inhibit the action of vitamin K which is a necessary cofactor for the enzyme that converts glutamic acid residues to γ -carboxyglutamic acid residues. This mechanism affects the clotting factors II, VII, IX, and X, as well as protein C and protein S.

A gene, genes, or gene pathway involved in the etiology of thrombosis or associated disorders or potential sites for targeted drug therapy of thrombosis are depicted in Table 11 with the specific gene list in Table 6. Current candidate therapeutic interventions in development for the treatment of thrombosis are listed in Table 64.

I. Renal Disease

The kidneys are primarily involved in regulating body fluid volume and composition by forming urine. The purpose of urine excretion, composed of ionic solutes, is to remove or eliminate metabolic end-products and maintain fluid volume and composition for the sustenance of physiologic function of the rest of the body. Urine formation and composition is affected by dietary intake of solutes and water as well as endogenous and exogenous carbohydrates, proteins, and nucleic acids. The kidneys also provide the mechanism to excrete drugs, toxins, and other exogenous substances.

Urine formation occurs via a sequence of five steps: 1) the glomerulus filters extracellular fluid across the glomerulus capillaries and the visceral epithelium of Bowman's capsule; the driving force is mean arterial blood pressure; 2) the proximal tubule isototically reabsorbs approximately two-thirds of the glomerular filtrate; 3) the loop of Henle dissociates the absorption of sodium and water; 4) the distal convoluted tubule primarily absorbs sodium under the influence of aldosterone and secretes protons, ammonia, and potassium; and lastly, 5) the collecting duct system regulates the osmolarity of urine under the influence of antidiuretic hormone. In addition to its function of producing urine, the kidney can also serve as an endocrine organ producing and secreting prostaglandins, kallikrein-kinins, erythropoietin, and renin. The kidney also has a function and role in metabolism. The kidney is a target organ for many hormones including parathyroid hormone, aldosterone, and antidiuretic hormone.

Renal dysfunction or disorders often are clinically nonspecific and are characterized by hematuria, azotemia, hypertension, and metabolic acidosis. Broadly, kidney dysfunction can be categorized as underperfusion syndromes, renal parenchymal syndromes, and post-renal syndromes.

Renal underperfusion syndromes include reduced effective circulating volume (including circulatory collapse, congestive heart failure, and cirrhosis of the liver), occlusive renal artery disease (including renal artery atherosclerosis, fibromuscular hyperplasia), and vasoconstriction of renal microvasculature (including acute transplant rejection, cyclosporin nephrotoxicity, and amphotericin B nephrotoxicity).

Renal parenchymal syndromes include acute hypertensive nephropathy, analgesic nephropathy, hemolytic-uremic syndrome, hypercalcemic nephropathy, interstitial nephritis, lupus nephritis, multiple myeloma, oxalate nephropathy, pyelonephritis, glomerulonephritis, renal vein thrombosis, Wegener's granulomatosis.

Renal failure, or the uremic syndrome, occurs when the functional renal mass is sufficiently reduced such that the kidney is longer able to conduct normal functions. Thus, the clinical hallmarks of this disease are related to the loss of urine formation, excretion, and aberrant composition of body fluids as well as loss of erythropoietin and renin and may be treated separately. These related disorders include electrolyte disorders (accumulation of potassium, sodium, phosphate, magnesium and aluminum and hypocalcemia), cardiovascular abnormalities (including accelerated atherosclerosis, hypertension, pericarditis, myocardial dysfunction), hematologic dysfunction (including anemia, leukocyte dysfunction, hemorrhagic diathesis), gastrointestinal disorders (including anorexia, nausea,

vomiting, gastroparesis, gastrointestinal bleeding), disorders of taste, renal osteodystrophy (including osteomalacia, osteitis fibrosa, osteosclerosis, osteoporosis), neurologic abnormalities (including insomnia, fatigue, psychological symptoms, asterixis, peripheral neuropathies), myopathy, impaired carbohydrate intolerance (peripheral resistance to insulin)), endocrine and metabolic disorders (including glucose intolerance, insulin resistance, insulin degradation, hypoglycemia, fertility disorders, hypothermia), hyperuricemia, and pruritis, soft tissue calcification and uremic frost. In chronic renal failure, the loss of renal function may be associated with adaptive functional changes in an attempt to restore renal function. These adaptive processes include increased glomerular filtration rate of the intact nephrons, and increased phosphate excretion. Unfortunately, as the kidney disease and the loss of renal function progresses, these adaptive processes may ultimately create more damage than restore function.

In any of the cases for renal disease there are aggravating factors that can affect the progression of the disease including vascular volume depletion (as a result of diuretics, gastrointestinal fluid losses, dehydration, low cardiac output, renal hypoperfusion, atheroembolic disease, ascites, nephrotic syndrome), drugs (including aminoglycosides, prostaglandin synthesis inhibitors, diuretics), obstructions (including tubule obstruction via uric acid or Bence Jones protein or posttubular obstruction via prostatic hypertrophy, necrotic papillae, or ureteral stones), infections, toxins (including radiographic contrast materials), hypertensive crisis, and hypercalcemia or hyperphosphatemia.

Treatments of renal disease are dependent on whether there is an acute or chronic condition. In the acute conditions, stabilization of fluid and electrolyte balance is critical for the sustenance of life. In chronic end-stage failure the patient may have to depend on exogenous dialysis or transplantation.

A gene, genes, or gene pathway involved in the etiology of renal disease or associated disorders or potential sites for targeted drug therapy of renal disease or associated disorders are depicted in Table 11 with the specific gene list in Table 6. Current candidate therapeutic interventions in development for the treatment of anemia are listed in Table 57, for renal disease in Table 65, and for nephritis in Table 66.

J. Restenosis

Interventional cardiology includes procedures aimed at mechanically improving coronary blood flow. These procedures include intracoronary stents, coronary artery bypass surgery, and percutaneous transluminal coronary angioplasty (PCTA). Although successful resolution of coronary arterial vessel occlusion has

been accomplished with PCTA in as many as two thirds of the patients, currently nearly 20-30% of the patients require emergency bypass surgery, there is an associated 4-10% mortality, 2-5% sustain damage to the vessel including dissection, intimal disruption, perforation, and embolism, and 9% experience Q-wave infarctions. Another PCTA related complication is coronary restenosis. Restenosis, or reocclusion of the coronary vessel, has predisposing factors including male gender, continued smoking after PCTA, diabetes mellitus, elevated insulin levels, absence or previous myocardial infarction, and unstable angina.

A gene, genes, or gene pathway involved in the etiology of restenosis or associated disorders or potential sites for targeted drug therapy of restenosis are depicted in Table 11 with the specific gene list in Table 6. Current candidate therapeutic interventions in development for the treatment of restenosis are listed in Table 67.

K. Peripheral vascular disease

Peripheral vascular disease (PVD) refers to diseases of any of the blood vessels outside the myocardium and to diseases of the lymph vessels. The disorder is often a narrowing of the blood vessels that carry blood to the arms and legs. There are two types of PVD, functional PVD and organic PVD. Functional PVD is not organic and does not involve defects in the structure of the blood vessels. Functional PVD includes Raynaud's syndrome. Organic PVD are caused by structural changes in the vessel, such as inflammation and tissue damage, for example Buerger's disease. PVD can result from atheromatous narrowing of the arteries to the legs. Symptoms may range from calf pain on exercise "intermittent claudication", to rest pain and gangrene. Intermittent claudication is the commonest symptom occurring in around up to 5% of men and 2.5% of women aged 60 or over. Peripheral vascular disease may be the result of venous stasis, anemia, dysbetalipoproteinemia, diabetes mellitus, and systemic sclerosis.

A gene, genes, or gene pathway involved in the etiology of peripheral vascular disease or associated disorders or potential sites for targeted drug therapy of peripheral vascular disease are depicted in Table 11 with the specific gene list in Table 6. Current candidate therapeutic interventions in development for the treatment of peripheral vascular disease are listed in Table 68.

Advantages of Pharmacogenomic Clinical Development of Novel Candidate Therapeutic Interventions for the Treatment of Disease

The evidence that a variance in a gene involved in a pathway that affects drug response, indicates and supports the theory that there is a likelihood that other genes have similar qualities to various degrees. As drug research and development proceeds to identify more lead candidate therapeutic interventions for neurologic and psychiatric disease, there is possible utility in stratifying patients based upon their genotype for these yet to be correlated variances. Further, as described in the Detailed Description, methods for the identification of candidate genes and gene pathways, stratification, clinical trial design, and implementation of genotyping for appropriate medical management of a given disease is easily translated for patients with neurologic and psychiatric disease. As described below there are likely gene pathways as are those that are outlined in the gene pathway Tables 1-6 as described above and matrix Tables 7-11.

The advantages of a clinical research and drug development program that include the use of polymorphic genotyping for the stratification of patients for the appropriate selection of candidate therapeutic intervention includes 1) identification of patients that may respond earlier to therapy, 2) identification of the primary gene and relevant polymorphic variance that directly affects efficacy, safety, or both, 3) identification of pathophysiologic relevant variance or variances and potential therapies affecting those allelic genotypes or haplotypes, and 4) identification of allelic variances or haplotypes in genes that indirectly affects efficacy, safety or both.

Based upon these advantages, designing and performing a clinical trial, either prospective or retrospective, which includes a genotype stratification arm will incorporate analysis of clinical outcomes and potential genetic variation associated with those outcomes, and hypothesis testing of the statistically relevant correlation of the genotypic stratification and therapeutic benefits. If statistical relevance is detectable, these studies will be incorporated into regulatory filings. Ultimately, these clinical trial data will be considered during the approval for marketing process, as well as, incorporated into accepted medical management of the described indications.

By identifying subsets of patients diagnosed with anxiety that respond earlier to agents, optimal candidate therapeutic interventions may reduce the lag time prior to relief of psychiatric symptoms. Appropriate genotyping and correlation to dosing regimen would be beneficial to the patient, caregivers, medical personnel, and the patient's loved ones.

As an example of identification of the primary gene and relevant polymorphic variance that directly affects efficacy, safety, or both one could select a gene pathway as described in the Detailed Description, and determine the effect of

genetic polymorphism and therapy efficacy, safety, or both within that given pathway. By embarking on the previously described gene pathway approach, it is technically feasible to determine the relevant genes within such a targeted drug development program for the clinical indications described in this invention.

5 Identification of pathophysiologic relevant variance or variances and potential therapies affecting those allelic genotypes or haplotypes will speed the drug development. There is a need for therapies that are targeted to the disease and symptom management with limited or no undesirable side effects. Identification of a specific variance or variances within genes involved in the pathophysiologic
10 manifestation of anxiety and specific genetic polymorphisms of these critical genes can assist the development of novel anxiolytic agents and the identification of those patients that may best benefit from therapy of these candidate therapeutic alternatives.

By identifying allelic variances or haplotypes in genes that indirectly affects
15 efficacy, safety or both one could target specific secondary drug or agent therapeutic actions that affect the overall therapeutic action of conventional, atypical, or novel action.

In Tables 12-17 and 18-23, there is a listing of candidate genes and specific single nucleotide polymorphisms that may be critical for the identification and
20 stratification of an anxiety patient population based upon genotype. In matrix Tables 7-11 one skilled in the art would be able to identify these pathway specific genes or other genes listed in Tables 7-11 that may be involved in the manifestation of neurologic or psychiatric disease or are likely candidate targets for therapeutic approaches described in this invention.

25 A sample of therapies approved or in development for preventing or treating the progression of symptoms of cancer currently known in the art are shown in Table 24; for neurologic and psychiatric disease, Tables 25-36; for inflammation and immune disorders, Tables 38-49; for endocrine and metabolic disease, Tables 50-56; and for cardiovascular and renal disease, Tables 57-68. In these tables, the candidate
30 therapeutics were sorted and listed by mechanism of action. Further, the product name, the pharmacologic mechanism of action, chemical name (if specified), and the indication is listed as well.

Pharmacogenomics studies for these drugs, as well as other agents, drugs,
35 compounds or candidate therapeutic interventions, could be performed by identifying genes that are involved in the function of a drug including, but not limited to is absorption, distribution metabolism, or elimination, the interaction of the drug with its target as well as potential alternative targets, the response of the cell to the binding of a drug to a target, the metabolism (including synthesis,

biodistribution or elimination) of natural compounds which may alter the activity of the drug by complementary, competitive or allosteric mechanisms that potentiate or limit the effect of the drug, and genes involved in the etiology of the disease that alter its response to a particular class of therapeutic agents. It will be recognized to those skilled in the art that this broadly includes proteins involved in pharmacokinetics as well as genes involved in pharmacodynamics. This also includes genes that encode proteins homologous to the proteins believed to carry out the above functions, which are also worth evaluation as they may carry out similar functions. Together the foregoing proteins constitute the candidate genes for affecting response of a patient to the therapeutic intervention. Using the methods described above, variances in these genes can be identified, and research and clinical studies can be performed to establish an association between a drug response or toxicity and specific variances.

For each of the described disease indications one skilled in the art can identify novel candidate therapeutic interventions that may be used to treat the disease or symptoms and/or proceed with a regimen of palliative care. For compounds that have yet to achieve approval, or are still in development one skilled in the art can determine those candidate therapeutic interventions that may be of therapeutic benefit.

Exemplary compounds in development for the treatment of disease disorders or dysfunctions

There are many sources for obtaining information on drugs approved for human therapeutic use and for those compounds under clinical or preclinical investigation, as well as for compounds which have been identified as having a particular pharmacological activity. For products, which have been approved, the PDR contains a listing of the package inserts for all of the products available for human therapeutic intervention. The Merck Index can be used as an additional text to supplement information gathered on the candidate therapeutic interventions. For products that are under clinical or preclinical development, there are databases cataloging information on those candidate therapeutic interventions. Generally that information includes aspects of the drug development process, such as phase of development, identified therapeutic indications, name of manufacturer, mechanistic and pharmacological activities of the product. These databases are available for a fee, and include: PharmaProjects (<http://pibpubs.co.uk/pharmamain2/html>) and R&D Focus (http://www.ims.global.com/products/lifecycle/r_and_d.htm). One skilled in the art can readily utilize these sources to determine appropriate candidate therapeutic intervention for the identified disease, disorder or condition.

Since there are a large number of candidate therapeutic interventions that are either approved for human therapeutic use or under clinical or preclinical investigation, one skilled in the art could search through publicly available or fee-for-access databases for interventions that may be of therapeutic benefit for a particular disease, disorder, or condition, and determine whether variances in particular genes correlate with interpatient variation in response to one or more of those therapeutic interventions. An example of the results of such searching is provided in Tables 24-68. In these tables, the disease, disorder or condition is listed. In order to generate a table or other compendium of information as listed in the table, one skilled in the art can search, for example as for Table 35, in databases for products having the indication "schizophrenia". Alternatively, one can search for alternative indications or co-morbidities, e.g., psychoses, neuroleptic, neurological to arrive at a more complete list of the available products. In the table, the candidate therapeutics were sorted and listed by pharmacologic mechanism of action (action). Further, the product name, chemical name (if specified), as well as the indication considered for clinical development. If the candidate therapeutic interventions are approved for therapeutic use, then one skilled in the art can obtain dosing, adverse events, pharmacologic parameters (both pharmacokinetic and pharmacodynamic), and clinical data or information by referring to the PDR. If the candidate therapeutic intervention are in clinical or preclinical stages of drug development, then one skilled in the art would gather data on dosing, adverse events, pharmacologic parameters (both pharmacokinetic and pharmacodynamic), and clinical data or information for the drug or product sponsor. In both cases, selection of a candidate therapeutic intervention for retrospective or prospective pharmacogenetic clinical studies would use an analysis of the likelihood that there is a phenomenological or statistical support for the review of the data to ascertain whether the candidate therapeutic intervention (approved or in development) efficacy or safety profiles can be grouped based upon the individual's genotype or phenotype. In this way, a gene or genes selected, e.g., from a pathway involving the cellular or more broadly the pharmacological mechanism of actions, can be identified and genotyping can be performed in order to determine the allelic variance, variances, for haplotype. Further, one could group the individuals by such genetic variances and further by the therapeutic outcome determinants.

Pharmacogenomics studies for these drugs, as well as other agents, drugs, compounds or candidate therapeutic interventions, can be performed by identifying genes that are involved in the the function of a drug including, but not limited to is absorption, distribution metabolism, or elimination , the interaction of the drug with its target as well as potential alternative targets, the response of the cell to the

binding of a drug to a target, the metabolism (including synthesis, biodistribution or elimination) of natural compounds which may alter the activity of the drug by complementary, competitive or allosteric mechanisms that potentiate or limit the effect of the drug, and genes involved in the etiology of the disease that alter its response to a particular class of therapeutic agents. It will be recognized to those skilled in the art that this broadly includes proteins involved in pharmacokinetics as well as genes involved in pharmacodynamics. This also includes genes that encode proteins homologous to the proteins believed to carry out the above functions, which are also worth evaluation as they may carry out similar functions. Together the foregoing proteins constitute the candidate genes for affecting response of a patient to the therapeutic intervention. Using the methods described above, variances in these genes can be identified, and research and clinical studies can be performed to establish an association between a drug response or toxicity and specific variances.

Further, there may be genes within pathways that are either involved in metabolism of drugs, hormones, compounds, agents, or neurotransmitters or are involved in metabolism of various drugs or compounds. In Tables 1-6 and 12-23, there are listings of candidate genes and specific single nucleotide polymorphisms that may be critical for the identification and stratification of a patient population diagnosed with neurologic or psychiatric disease based upon genotype. Current pathways that may have involvement in the therapeutic benefit of described disease indications of this invention are listed as gene pathways and are listed in Tables 1-23. One skilled in the art would be able to identify these pathway specific gene or genes that may be involved in the manifestation of the described neurological or psychiatric disease, are likely candidate targets for novel therapeutic approaches, or are involved in mediating patient population differences in drug response to therapies for neurological or psychiatric disease described in the present invention.

As indicated in the Summary above, certain aspects of the present invention typically involve the following process, which need not occur separately or in the order stated. Not all of these described processes must be present in a particular method, or need be performed by a single entity or organization or person. Additionally, if certain of the information is available from other sources, that information can be utilized in the present invention. The processes are as follows:

- a) variability between patients in the response to a particular treatment is observed;
- b) at least a portion of the variable response is correlated with the presence or absence of at least one variance in at least one gene;
- c) an analytical or diagnostic test is provided to determine the presence or absence of the at least one variance in individual patients;
- d) the presence or absence of the variance or variances is used

to select a patient for a treatment or to select a treatment for a patient, or the variance information is used in other methods described herein.

A. Identification of Interpatient Variability in Response to a Treatment

5 Interpatient variability is the rule, not the exception, in clinical therapeutics. One of the best sources of information on interpatient variability is the nurses and physicians supervising the clinical trial who accumulate a body of first hand observations of physiological responses to the drug in different normal subjects or patients. Evidence of interpatient variation in response can also be measured
10 statistically, and may be best assessed by descriptive statistical measures that examine variation in response (beneficial or adverse) across a large number of subjects, including in different patient subgroups (men vs. women; whites vs. blacks; Northern Europeans vs. Southern Europeans, etc.).

In accord with the other portions of this description, the present invention concerns
15 DNA sequence variances that can affect one or more of:

i. The susceptibility of individuals to a disease;

ii. The course or natural history of a disease;

iii. The response of a patient with a disease to a medical intervention, such as, for example, a drug, a biologic substance, physical energy such as radiation therapy, or
20 a specific dietary regimen. (The terms 'drug', 'compound' or 'treatment' as used herein may refer to any of the foregoing medical interventions.) The ability to predict either beneficial or detrimental responses is medically useful.

Thus variation in any of these three parameters may constitute the basis for initiating a pharmacogenetic study directed to the identification of the genetic
25 sources of interpatient variation. The effect of a DNA sequence variance or variances on disease susceptibility or natural history (i and ii, above) are of particular interest as the variances can be used to define patient subsets which behave differently in response to medical interventions such as those described in (iii). The methods of this invention are also useful in a clinical development
30 program where there is not yet evidence of interpatient variation (perhaps because the compound is just entering clinical trials) but such variation in response can be reliably anticipated. It is more economical to design pharmacogenetic studies from the beginning of a clinical development program than to start at a later stage when

the costs of any delay are likely to be high given the resources typically committed to such a program.

In other words, a variance can be useful for customizing medical therapy at least for either of two reasons. First, the variance may be associated with a specific disease subset that behaves differently with respect to one or more therapeutic interventions (i and ii above); second, the variance may affect response to a specific therapeutic intervention (iii above). Consider for exemplary purposes pharmacological therapeutic interventions. In the first case, there may be no effect of a particular gene sequence variance on the observable pharmacological action of a drug, yet the disease subsets defined by the variance or variances differ in their response to the drug because, for example, the drug acts on a pathway that is more relevant to disease pathophysiology in one variance-defined patient subset than in another variance-defined patient subset. The second type of useful gene sequence variance affects the pharmacological action of a drug or other treatment. Effects on pharmacological responses fall generally into two categories; pharmacokinetic and pharmacodynamic effects. These effects have been defined as follows in Goodman and Gilman's Pharmacologic Basis of Therapeutics (ninth edition, McGraw Hill, New York, 1986): "Pharmacokinetics" deals with the absorption, distribution, biotransformations and excretion of drugs. The study of the biochemical and physiological effects of drugs and their mechanisms of action is termed "pharmacodynamics."

Useful gene sequence variances for this invention can be described as variances which partition patients into two or more groups that respond differently to a therapy or that correlate with differences in disease susceptibility or progression, regardless of the reason for the difference, and regardless of whether the reason for the difference is known. The latter is true because it is possible, with genetic methods, to establish reliable associations even in the absence of a pathophysiological hypothesis linking a gene to a phenotype, such as a pharmacological response, disease susceptibility or disease prognosis.

B. Identification of Specific Genes and Correlation of Variances in Those Genes with Response to Treatment of Diseases or Conditions

It is useful to identify particular genes which do or are likely to mediate the efficacy or safety of a treatment method for a disease or condition, particularly in view of the large number of genes which have been identified and which continue to be identified in humans. As is further discussed in section C below, this correlation

can proceed by different paths. One exemplary method utilizes prior information on the pharmacology or pharmacokinetics or pharmacodynamics of a treatment method, e.g., the action of a drug, which indicates that a particular gene is, or is likely to be, involved in the action of the treatment method, and further suggests that variances in the gene may contribute to variable response to the treatment method. For example if a compound is known to be glucuronidated then a glucuronyltransferase is likely involved. If the compound is a phenol, the likely glucuronyltransferase is UGT1 (either the UGT1*1 or UGT1*6 transcripts, both of which catalyze the conjugation of planar phenols with glucuronic acid). Similar inferences can be made for many other biotransformation reactions.

Alternatively, if such information is not known, variances in a gene can be correlated empirically with treatment response. In this method, variances in a gene which exist in a population can be identified. The presence of the different variances or haplotypes in individuals of a study group, which is preferably representative of a population or populations of known geographic, ethnic and/or racial background, is determined. This variance information is then correlated with treatment response of the various individuals as an indication that genetic variability in the gene is at least partially responsible for differential treatment response. It may be useful to independently analyze variances in the different geographic, ethnic and/or racial groups as the presence of different genetic variances in these groups (i.e. different genetic background) may influence the effect of a specific variance. That is, there may be a gene x gene interaction involving one unstudied gene, however the indicated demographic variables may act as a surrogate for the unstudied allele. Statistical measures known to those skilled in the art are preferably used to measure the fraction of interpatient variation attributable to any one variance, or to measure the response rates in different subgroups defined genetically or defined by some combination of genetic, demographic and clinical criteria.

Useful methods for identifying genes relevant to the pharmacological action of a drug or other treatment are known to those skilled in the art, and include review of the scientific literature combined with inferential or deductive reasoning that one skilled in the art of molecular pharmacology and molecular biology would be capable of; large scale analysis of gene expression in cells treated with the drug compared to control cells; large scale analysis of the protein expression pattern in treated vs. untreated cells, or the use of techniques for identification of interacting proteins or ligand-protein interactions, such as yeast two-hybrid systems.

C. Development of a Diagnostic Test to Determine Variance Status

In accordance with the description in the Summary above, the present invention generally concerns the identification of variances in genes which are indicative of the effectiveness of a treatment in a patient. The identification of specific variances, in effect, can be used as a diagnostic or prognostic test.

Correlation of treatment efficacy and/or toxicity with particular genes and gene families or pathways is provided in Stanton et al., U.S. Provisional Application 60/093,484, filed July 20, 1998, entitled GENE SEQUENCE VARIANCES WITH UTILITY IN DETERMINING THE TREATMENT OF DISEASE (concerns the safety and efficacy of compounds active on folate or pyrimidine metabolism or action) and Stanton, U.S. Provisional Application No. 60/121,047, filed February 22, 1999, entitled GENE SEQUENCE VARIANCES WITH UTILITY IN DETERMINING THE TREATMENT OF DISEASE (concerning Alzheimer's disease and other dementias and cognitive disorders), which are hereby incorporated by reference in their entireties including drawings.

Genes identified in the examples below and in the Tables can be used in the methods of the present invention. A variety of genes which the inventors realize may account for interpatient variation in response to treatments for neurological and psychiatric diseases, conditions, disorders, and/or the development of same are listed in Tables 1-6, and 12-23. Gene sequence variances in said genes are particularly useful for aspects of the present invention.

Methods for diagnostic tests are well known in the art. Generally in this invention, the diagnostic test involves determining whether an individual has a variance or variant form of a gene that is involved in the disease or condition or the action of the drug or other treatment or effects of such treatment. Such a variance or variant form of the gene is preferably one of several different variances or forms of the gene that have been identified within the population and are known to be present at a certain frequency. In an exemplary method, the diagnostic test involves determining the sequence of at least one variance in at least one gene after amplifying a segment of said gene using a DNA amplification method such as the polymerase chain reaction (PCR). In this method DNA for analysis is obtained by amplifying a segment of DNA or RNA (generally after converting the RNA to cDNA) spanning one or more variances in the gene sequence. Preferably, the amplified segment is <500 bases in length, in an alternative embodiment the amplified segment is <100 bases in length, most preferably <45 bases in length.

In some cases it will be desirable to determine a haplotype instead of a genotype. In such a case the diagnostic test is performed by amplifying a segment of DNA or RNA (cDNA) spanning more than one variance in the gene sequence and

preferably maintaining the phase of the variances on each allele. The term "phase" refers to the relationship of variances on a single chromosomal copy of the gene, such as the copy transmitted from the mother (maternal copy or maternal allele) or the father (paternal copy or paternal allele). The haplotyping test may take part in two phases, where first genotyping tests at two or more variant sites reveal which sites are heterozygous in each patient or normal subject. Subsequently the phase of the two or more variant sites can be determined. In performing a haplotyping test preferably the amplified segment is >500 bases in length, more preferably it is >1,000 bases in length, and most preferably it is >2,500 bases in length. One way of preserving phase is to amplify one strand in the PCR reaction. This can be done using one or a pair of oligonucleotide primers that terminate (i.e. have a 3' end that stops) opposite the variant site, such that one primer is perfectly complementary to one variant form and the other primer is perfectly complementary to the other variant form. Other than the difference in the 3' most nucleotide the two primers are identical (forming an allelic primer pair). Only one of the allelic primers is used in any PCR reaction, depending on which strand is being amplified. The primer for the opposite strand may also be an allelic primer, or it may prime from a non-polymorphic region of the template. This method exploits the requirement of most polymerases for perfect complementarity at the 3' terminus of the primer in a primer-template complex. See, for example: Lo YM, Patel P, Newton CR, Markham AF, Fleming KA and JS Wainscoat. (1991) Direct haplotype determination by double ARMS: specificity, sensitivity and genetic applications. *Nucleic Acids Res* July 11;19(13):3561-7.

It is apparent that such diagnostic tests are performed after initial identification of variances within the gene, which allows selection of appropriate allele specific primers.

Diagnostic genetic tests useful for practicing this invention belong to two types: genotyping tests and haplotyping tests. A genotyping test simply provides the status of a variance or variances in a subject or patient. For example suppose nucleotide 150 of hypothetical gene X on an autosomal chromosome is an adenine (A) or a guanine (G) base. The possible genotypes in any individual are AA, AG or GG at nucleotide 150 of gene X.

In a haplotyping test there is at least one additional variance in gene X, say at nucleotide 810, which varies in the population as cytosine (C) or thymine (T). Thus a particular copy of gene X may have any of the following combinations of nucleotides at positions 150 and 810: 150A-810C, 150A-810T, 150G-810C or 150G-810T. Each of the four possibilities is a unique haplotype. If the two nucleotides interact in either RNA or protein, then knowing the haplotype can be

important. The point of a haplotyping test is to determine the haplotypes present in a DNA or cDNA sample (e.g. from a patient). In the example provided there are only four possible haplotypes, but, depending on the number of variances in the gene and their distribution in human populations there may be three, four, five, six or
5 more haplotypes at a given gene. The most useful haplotypes for this invention are those which occur commonly in the population being treated for a disease or condition. Preferably such haplotypes occur in at least 5% of the population, more preferably in at least 10%, still more preferably in at least 20% of the population and most preferably in at least 30% or more of the population. Conversely, when the
10 goal of a pharmacogenetic program is to identify a relatively rare population that has an adverse reaction to a treatment, the most useful haplotypes may be rare haplotypes, which may occur in less than 5%, less than 2%, or even in less than 1% of the population. One skilled in the art will recognize that the frequency of the adverse reaction provides a useful guide to the likely frequency of salient causative
15 haplotypes.

Based on the identification of variances or variant forms of a gene, a diagnostic test utilizing methods known in the art can be used to determine whether a particular form of the gene, containing specific variances or haplotypes, or combinations of variances and haplotypes, is present in at least one copy, one copy,
20 or more than one copy in an individual. Such tests are commonly performed using DNA or RNA collected from blood, cells, tissue scrapings or other cellular materials, and can be performed by a variety of methods including, but not limited to, PCR based methods, hybridization with allele-specific probes, enzymatic mutation detection, chemical cleavage of mismatches, mass spectrometry or DNA
25 sequencing, including minisequencing. Methods for haplotyping are described above. In particular embodiments, hybridization with allele specific probes can be conducted in two formats: (1) allele specific oligonucleotides bound to a solid phase (glass, silicon, nylon membranes) and the labelled sample in solution, as in many DNA chip applications, or (2) bound sample (often cloned DNA or PCR amplified
30 DNA) and labelled oligonucleotides in solution (either allele specific or short – e.g. 7mers or 8mers - so as to allow sequencing by hybridization). Preferred methods for diagnostic testing of variances are described in four patent applications Stanton et al, entitled A METHOD FOR ANALYZING POLYNUCLEOTIDES, serial numbers
09/394,467; 09/394,457; 09/394,774; and 09/394,387; all filed September 10, 1999.
35 The application of such diagnostic tests is possible after identification of variances that occur in the population. Diagnostic tests may involve a panel of variances from one or more genes, often on a solid support, which enables the simultaneous determination of more than one variance in one or more genes.

D. Use of Variance Status to Determine Treatment

The present disclosure describes exemplary gene sequence variances in genes identified in a gene table herein (e.g., Tables 12-17 and 18-23), and variant forms of these gene that may be determined using diagnostic tests. As indicated in the Summary, such a variance-based diagnostic test can be used to determine whether or not to administer a specific drug or other treatment to a patient for treatment of a disease or condition. Preferably such diagnostic tests are incorporated in texts such as are described in Clinical Diagnosis and Management by Laboratory Methods (19th Ed) by John B. Henry (Editor) W B Saunders Company, 1996; Clinical Laboratory Medicine : Clinical Application of Laboratory Data, (6th edition) by R. Ravel, Mosby-Year Book, 1995, or other medical textbooks including, without limitation, textbooks of medicine, laboratory medicine, therapeutics, pharmacy, pharmacology, nutrition, allopathic, homeopathic, and osteopathic medicine; preferably such a test is developed as a 'home brew' method by a certified diagnostic laboratory; most preferably such a diagnostic test is approved by regulatory authorities, e.g., by the U.S. Food and Drug Administration, and is incorporated in the label or insert for a therapeutic compound, as well as in the Physicians Desk Reference.

In such cases, the procedure for using the drug is restricted or limited on the basis of a diagnostic test for determining the presence of a variance or variant form of a gene. Alternatively the use of a genetic test may be advised as best medical practice, but not absolutely required, or it may be required in a subset of patients, e.g. those using one or more other drugs, or those with impaired liver or kidney function. The procedure that is dictated or recommended based on genotype may include the route of administration of the drug, the dosage form, dosage, schedule of administration or use with other drugs; any or all of these may require selecting or determination consistent with the results of the diagnostic test or a plurality of such tests. Preferably the use of such diagnostic tests to determine the procedure for administration of a drug is incorporated in a text such as those listed above, or medical textbooks, for example, textbooks of medicine, laboratory medicine, therapeutics, pharmacy, pharmacology, nutrition, allopathic, homeopathic, and osteopathic medicine. As previously stated, preferably such a diagnostic test or tests are required by regulatory authorities and are incorporated in the label or insert as well as the Physicians Desk Reference.

Variances and variant forms of genes useful in conjunction with treatment methods may be associated with the origin or the pathogenesis of a disease or condition. In many useful cases, the variant form of the gene is associated with a

specific characteristic of the disease or condition that is the target of a treatment, most preferably response to specific drugs or other treatments. Examples of diseases or conditions ameliorable by the methods of this invention are identified in the Examples and tables below; in general treatment of disease with current methods, particularly drug treatment, always involves some unknown element (involving efficacy or toxicity or both) that can be reduced by appropriate diagnostic methods.

Alternatively, the gene is involved in drug action, and the variant forms of the gene are associated with variability in the action of the drug. For example, in some cases, one variant form of the gene is associated with the action of the drug such that the drug will be effective in an individual who inherits one or two copies of that form of the gene. Alternatively, a variant form of the gene is associated with the action of the drug such that the drug will be toxic or otherwise contra-indicated in an individual who inherits one or two copies of that form of the gene.

In accord with this invention, diagnostic tests for variances and variant forms of genes as described above can be used in clinical trials to demonstrate the safety and efficacy of a drug in a specific population. As a result, in the case of drugs which show variability in patient response correlated with the presence or absence of a variance or variances, it is preferable that such drug is approved for sale or use by regulatory agencies with the recommendation or requirement that a diagnostic test be performed for a specific variance or variant form of a gene which identifies specific populations in which the drug will be safe and/or effective. For example, the drug may be approved for sale or use by regulatory agencies with the specification that a diagnostic test be performed for a specific variance or variant form of a gene which identifies specific populations in which the drug will be toxic. Thus, approved use of the drug, or the procedure for use of the drug, can be limited by a diagnostic test for such variances or variant forms of a gene; or such a diagnostic test may be considered good medical practice, but not absolutely required for use of the drug.

As indicated, diagnostic tests for variances as described in this invention may be used in clinical trials to establish the safety and efficacy of a drug. Methods for such clinical trials are described below and/or are known in the art and are described in standard textbooks. For example, diagnostic tests for a specific variance or variant form of a gene may be incorporated in the clinical trial protocol as inclusion or exclusion criteria for enrollment in the trial, to allocate certain patients to treatment or control groups within the clinical trial or to assign patients to different treatment cohorts. Alternatively, diagnostic tests for specific variances may be performed on all patients within a clinical trial, and statistical analysis performed comparing and contrasting the efficacy or safety of a drug between individuals with

different variances or variant forms of the gene or genes. Preferred embodiments involving clinical trials include the genetic stratification strategies, phases, statistical analyses, sizes, and other parameters as described herein.

Similarly, diagnostic tests for variances can be performed on groups of patients known to have efficacious responses to the drug to identify differences in the frequency of variances between responders and non-responders. Likewise, in other cases, diagnostic tests for variance are performed on groups of patients known to have toxic responses to the drug to identify differences in the frequency of the variance between those having adverse events and those not having adverse events. Such outlier analyses may be particularly useful if a limited number of patient samples are available for analysis. It is apparent that such clinical trials can be or are performed after identifying specific variances or variant forms of the gene in the population. In defining outliers it is useful to examine the distribution of responses in the placebo group; outliers should preferably have responses that exceed in magnitude the extreme responses in the placebo group.

The identification and confirmation of genetic variances is described in certain patents and patent applications. The description therein is useful in the identification of variances in the present invention. For example, a strategy for the development of anticancer agents having a high therapeutic index is described in Housman, International Application PCT/US94/08473 and Housman, INHIBITORS OF ALTERNATIVE ALLELES OF GENES ENCODING PROTEINS VITAL FOR CELL VIABILITY OR CELL GROWTH AS A BASIS FOR CANCER THERAPEUTIC AGENTS, U.S. Patent 5,702,890, issued December 30, 1997, which are hereby incorporated by reference in their entireties. Also, a number of gene targets and associated variances are identified in Housman et al., PCT/US98/05419, entitled TARGET ALLELES FOR ALLELE-SPECIFIC DRUGS, filed March 19, 1998, which is hereby incorporated by reference in its entirety, including drawings.

The described approach and techniques are applicable to a variety of other diseases, conditions, and/or treatments and to genes associated with the etiology and pathogenesis of such other diseases and conditions and the efficacy and safety of such other treatments.

Useful variances for this invention can be described generally as variances which partition patients into two or more groups that respond differently to a therapy (a therapeutic intervention), regardless of the reason for the difference, and regardless of whether the reason for the difference is known.

III. From Variance List to Clinical Trial: Identifying Genes and Gene Variances that Account for Variable Responses to Treatment

There are a variety of useful methods for identifying a subset of genes from a large set of candidate genes that should be prioritized for further investigation with respect to their influence on inter-individual variation in disease predisposition or response to a particular drug. These methods include for example, (1) searching the biomedical literature to identify genes relevant to a disease or the action of a drug, (2) screening the genes identified in step 1 for variances. A large set of exemplary variances are provided in Tables 12-23. Other methods include (3) using computational tools to predict the functional effects of variances in specific genes, (4) using *in vitro* or *in vivo* experiments to identify genes which may participate in the response to a drug or treatment, and to determine the variances which affect gene, RNA or protein function, and may therefore be important genetic variables affecting disease manifestations or drug response, and (5) retrospective or prospective clinical trials. Computational tools are described in U.S. Patent Application, Stanton et al., serial number, attorney docket number 241/034, filed April 26, 1999, entitled GENE SEQUENCE VARIANCES WITH UTILITY IN DETERMINING THE TREATMENT OF DISEASE, and in Stanton et al., Serial No. 09/419,705, filed October 14, 1999, entitled VARIANCE SCANNING METHOD FOR IDENTIFYING GENE SEQUENCE VARIANCES, which are hereby incorporated by reference in their entireties, including drawings. Other methods are considered below in some detail.

(1) To begin, one preferably identifies, for a given treatment, a set of candidate genes that are likely to affect disease phenotype or drug response. This can be accomplished most efficiently by first assembling the relevant medical, pharmacological and biological data from available sources (e.g., public databases and publications). One skilled in the art can review the literature (textbooks, monographs, journal articles) and online sources (databases) to identify genes most relevant to the action of a specific drug or other treatment, particularly with respect to its utility for treating a specific disease, as this beneficially allows the set of genes to be analyzed ultimately in clinical trials to be reduced from an initial large set. Specific strategies for conducting such searches are described below. In some instances the literature may provide adequate information to select genes to be studied in a clinical trial, but in other cases additional experimental investigations of the sort described below will be preferable to maximize the likelihood that the salient genes and variances are moved forward into clinical studies. Specific genes relevant to understanding

interpatient variation in response to treatments for major neurological and psychiatric diseases are listed in Tables 1-6. In Tables 7-11 preferred sets of genes for analysis of variable therapeutic response in specific diseases are highlighted. These genes are exemplary; they do not constitute a complete set of genes that may account for variation in clinical response. Experimental data are also useful in establishing a list of candidate genes, as described below.

(2) Having assembled a list of candidate genes generally the second step is to screen for variances in each candidate gene. Experimental and computational methods for variance detection are described in this invention, and tables of exemplary variances are provided (Tables 12-23) as well as methods for identifying additional variances and a written description of such possible additional variances in the cDNAs of genes that may affect drug action (see Stanton et al., Application No. 09/300,747, filed April 26, 1999, entitled GENE SEQUENCE VARIANCES WITH UTILITY IN DETERMINING THE TREATMENT OF DISEASE, incorporated in its entirety.

(3) Having identified variances in candidate genes the next step is to assess their likely contribution to clinical variation in patient response to therapy, preferably by using informatics-based approaches such as DNA and protein sequence analysis and protein modeling. The literature and informatics-based approaches provide the basis for prioritization of candidate genes, however it may in some cases be desirable to further narrow the list of candidate genes, or to measure experimentally the phenotype associated with specific variances or sets of variances (e.g. haplotypes).

(4) Thus, as a third step in candidate gene analysis, one skilled in the art may elect to perform *in vitro* or *in vivo* experiments to assess the functional importance of gene variances, using either biochemical or genetic tests. (Certain kinds of experiments – for example gene expression profiling and proteome analysis - may not only allow refinement of a candidate gene list but may also lead to identification of additional candidate genes.) Combination of two or all of the three above methods will provide sufficient information to narrow and prioritize the set of candidate genes and variances to a number that can be studied in a clinical trial with adequate statistical power.

(5) The fourth step is to design retrospective or prospective human clinical trials to test whether the identified allelic variance, variances, or haplotypes or combination thereof influence the efficacy or toxicity profiles for a given drug or

other therapeutic intervention. It should be recognized that this fourth step is the crucial step in producing the type of data that would justify introducing a diagnostic test for at least one variance into clinical use. Thus while each of the above four steps are useful in particular instances of the invention, this final step is indispensable. Further guidance and examples of how to perform these five steps are provided below.

(6) A fifth (optional) step entails methods for using a genotyping test in the promotion and marketing of a treatment method. It is widely appreciated that there is a tendency in the pharmaceutical industry to develop many compounds for well established therapeutic targets. Examples include beta adrenergic blockers, hydroxymethylglutaryl (HMG) CoA reductase inhibitors (statins), dopamine D2 receptor antagonists and serotonin transporter inhibitors. Frequently the pharmacology of these compounds is quite similar in terms of efficacy and side effects. Therefore the marketing of one compound vs. other members of the class is a challenging problem for drug companies, and is reflected in the lesser success that late products typically achieve compared to the first and second approved products. It occurred to the inventors that genetic stratification can provide the basis for identifying a patient population with a superior response rate or improved safety to one member of a class of drugs, and that this information can be the basis for commercialization of that compound. Such a commercialization campaign can be directed at caregivers, particularly physicians, or at patients and their families, or both.

1. Identification of Candidate Genes Relevant to the Action of a Drug

Practice of this invention will often begin with identification of a specific pharmaceutical product, for example a drug, that would benefit from improved efficacy or reduced toxicity or both, and the recognition that pharmacogenetic investigations as described herein provide a basis for achieving such improved characteristics. The question then becomes which genes and variances, such as those provided in this application in Tables 1-6, 12-17, and 18-23, would be most relevant to interpatient variation in response to the drug. As discussed above, the set of relevant genes includes both genes involved in the disease process and genes involved in the interaction of the patient and the treatment – for example genes involved in pharmacokinetic and pharmacodynamic action of a drug. The biological and biomedical literature and online databases provide useful guidance in selecting such genes. Specific guidance in the use of these resources is provided below.

Review the literature and online sources

One way to find genes that affect response to a drug in a particular disease setting is to review the published literature and available online databases regarding the pathophysiology of the disease and the pharmacology of the drug. Literature or
5 online sources can provide specific genes involved in the disease process or drug response, or describe biochemical pathways involving multiple genes, each of which may affect the disease process or drug response.

Alternatively, biochemical or pathological changes characteristic of the disease may be described; such information can be used by one skilled in the art to
10 infer a set of genes that can account for the biochemical or pathologic changes. For example, to understand variation in response to a drug that modulates serotonin levels in a central nervous system (CNS) disorder associated with altered levels of serotonin one would preferably study, at a minimum, variances in genes responsible for serotonin biosynthesis, release from the cell, receptor binding, presynaptic
15 reuptake, and degradation or metabolism. Genes responsible for each of these functions should be examined for variation that may account for interpatient differences in drug response or disease manifestations. As recognized by those skilled in the art, a comprehensive list of such genes can be obtained from textbooks, monographs and the literature.

20 There are several types of scientific information, described in some detail below, that are valuable for identifying a set of candidate genes to be investigated with respect to a specific disease and therapeutic intervention. First there is the medical literature, which provides basic information on disease pathophysiology and therapeutic interventions. A subset of this literature is devoted to specific
25 description of pathologic conditions. Second there is the pharmacology literature, which will provide additional information on the mechanism of action of a drug (pharmacodynamics) as well as its principal routes of metabolic transformation (pharmacokinetics) and the responsible proteins. Third there is the biomedical literature (principally genetics, physiology, biochemistry and molecular biology),
30 which provides more detailed information on metabolic pathways, protein structure and function and gene structure. Fourth, there are a variety of online databases that provide additional information on metabolic pathways, gene families, protein function and other subjects relevant to selecting a set of genes that are likely to affect the response to a treatment.

Medical Literature

A good starting place for information on molecular pathophysiology of a specific disease is a general medical textbook such as Harrison's Principles of Internal Medicine, 14th edition, (2 Vol Set) by A.S. Fauci, E. Braunwald, K.J. Isselbacher, et al. (editors), McGraw Hill, 1997, or Cecil Textbook of Medicine (20th Ed) by R. L. Cecil, F. Plum and J. C. Bennett (Editors) W B Saunders Co., 1996. For pediatric diseases texts such as Nelson Textbook of Pediatrics (15th edition) by R.E. Behrman, R.M. Kliegman, A.M. Arvin and W.E. Nelson (Editors), W B Saunders Co., 1995 or Oski's Principles and Practice of Pediatrics (3rd Edition) by J.A. Mamillan & F.A. Oski Lippincott-Raven, 1999 are useful introductions. For obstetrical and gynecological disorders texts such as Williams Obstetrics (20th Ed) by F.G. Cunningham, N.F. Gant, P.C. McDonald et al. (Editors), Appleton & Lange, 1997 provide general information on disease pathophysiology. For psychiatric disorders texts such as the Comprehensive Textbook of Psychiatry, VI (2 Vols) by H.I. Kaplan and B.J. Sadock (Editors), Lippincott, Williams & Wilkins, 1995, or The American Psychiatric Press Textbook of Psychiatry (3rd edition) by R.E. Hales, S.C. Yudofsky and J.A. Talbott (Editors) Amer Psychiatric Press, 1999 provide an overview of disease nosology, pathophysiological mechanisms and treatment regimens.

In addition to these general texts, there are a variety of more specialized medical texts that provide greater detail about specific disorders which can be utilized in developing a list of candidate genes and variances relevant to interpatient variation in response to a treatment. For example, within the field of medicine there are standard textbooks for each of the subspecialties. Some examples include:

Heart Disease: A Textbook of Cardiovascular Medicine (2 Volume set) by E. Braunwald (Editor), W B Saunders Co., 1996; Hurst's the Heart, Arteries and Veins (9th Ed) (2 Vol Set) by R.W. Alexander, R.C. Schlant, V. Fuster, W. Alexander and E.H. Sonnenblick (Editors) McGraw Hill, 1998; Principles of Neurology (6th edition) by R.D. Adams, M. Victor (editors), and A.H. Ropper (Contributor), McGraw Hill, 1996; Sleisenger & Fordtran's Gastrointestinal and Liver Disease: Pathophysiology, Diagnosis, Management (6th edition) by M. Feldman, B.F. Scharschmidt and M. Sleisenger (Editors), W B Saunders Co., 1997; Textbook of Rheumatology (5th edition) by W.N. Kelley, S. Ruddy, E.D. Harris Jr. and C.B. Sledge (Editors) (2 volume set) W B Saunders Co., 1997; Williams Textbook of Endocrinology (9th edition) by J.D. Wilson, D.W. Foster, H. M. Kronenberg and Larsen (Editors), W B Saunders Co., 1998; Wintrobe's Clinical Hematology (10th Ed) by G.R. Lee, J. Foerster (Editor) and J. Lukens (Editors) (2 Volumes) Lippincott, Williams & Wilkins, 1998; Cancer: Principles & Practice of Oncology

(5th edition) by V.T. Devita, S.A. Rosenberg and S. Hellman (editors), Lippincott-Raven Publishers, 1997; Principles of Pulmonary Medicine (3rd edition) by S.E. Weinberger & J Fletcher (Editors), W B Saunders Co., 1998; Diagnosis and Management of Renal Disease and Hypertension (2nd edition) by A.K. Mandal & J.C. Jennette (Editors), Carolina Academic Press, 1994. Massry & Glassock's Textbook of Nephrology (3rd edition) by S.G. Massry & R.J. Glassock (editors) Williams & Wilkins, 1995; The Management of Pain by J.J. Bonica, Lea and Febiger, 1992; Ophthalmology by M. Yanoff & J.S. Duker, Mosby Year Book, 1998; Clinical Ophthalmology: A Systemic Approach by J.J. Kanski, Butterworth-Heinemann, 1994; and Essential Otolaryngology by J.K. Lee Appleton and Lange 1998.

In addition to these subspecialty texts there are many textbooks and monographs that concern more restricted disease areas, or specific diseases. Such books provide more extensive coverage of pathophysiologic mechanisms and therapeutic options. The number of such books is too great to provide examples for all but a few diseases, however one skilled in the art will be able to readily identify relevant texts. One simple way to search for relevant titles is to use the search engine of an online bookseller such as <http://www.amazon.com> or <http://www.barnesandnoble.com> using the disease or drug (or the group of diseases or drugs to which they belong) as search terms. For example a search for asthma would turn up titles such as Asthma : Basic Mechanisms and Clinical Management (3rd edition) by P.J. Barnes, I.W. Rodger and N.C. Thomson (Editors), Academic Press, 1998 and Airways and Vascular Remodelling in Asthma and Cardiovascular Disease : Implications for Therapeutic Intervention, by C. Page & J. Black (Editors), Academic Press, 1994.

Pathology Literature

In addition to medical texts there are texts that specifically address disease etiology and pathologic changes associated with disease. A good general pathology text is Robbins Pathologic Basis of Disease (6th edition) by R.S. Cotran, V. Kumar, T. Collins and S.L. Robbins, W B Saunders Co., 1998. Specialized pathology texts exist for each organ system and for specific diseases, similar to medical texts. These texts are useful sources of information for one skilled in the art for developing lists of genes that may account for some of the known pathologic changes in disease tissue. Exemplary texts are as follows:

Bone Marrow Pathology 2nd edition, by B.J. Bain, I. Lampert. & D. Clark, Blackwell Science, 1996; Atlas of Renal Pathology by F.G. Silva, W.B. Saunders,

1999; Fundamentals of Toxicologic Pathology by W.M. Haschek and C.G. Rousseaux, Academic Press, 1997; Gastrointestinal Pathology by P. Chandrasoma, Appleton and Lange, 1998; Ophthalmic Pathology with Clinical Correlations by J. Sassani, Lippincott-Raven, 1997; Pathology of Bone and Joint Disorders by F. McCarthy, F.J. Frassica and A. Ross, W. B. Saunders, 1998; Pulmonary Pathology by M.A. Grippi, Lippincott-Raven, 1995; Neuropathology by D. Ellison, L. Chimelli, B. Harding, S. Love & J. Lowe, Mosby Year Book, 1997; Greenfield's Neuropathology 6th edition by J.G. Greenfield, P.L. Lantos & D.I. Graham, Edward Arnold, 1997.

Pharmacology, Pharmacogenetics and Pharmacy Literature

There are also both general and specialized texts and monographs on pharmacology that provide data on pharmacokinetics and pharmacodynamics of drugs. The discussion of pharmacodynamics (mechanism of action of the drug) in such texts is often supported by a review of the biochemical pathway or pathways that are affected by the drug. Also, proteins related to the target protein are often listed; it is important to account for variation in such proteins as the related proteins may be involved in drug pharmacology. For example, there are 14 known serotonin receptors. Various pharmacological serotonin agonists or antagonists have different affinities for these different receptors. Variation in a specific receptor may affect the pharmacology not only of drugs targeted to that receptor, but also drugs that are principally agonists or antagonists of different receptors. Such compounds may produce different effects on two allelic forms of a non-targeted receptor; for example on variant form may bind the compound with higher affinity than the other, or a compound that is principally an antagonist for one allele may be a partial agonist for another allele. Thus genes encoding proteins structurally related to the target protein should be screened for variance in order to successfully realize the methods of the present invention. A good general pharmacology text is Goodman & Gilman's the Pharmacological Basis of Therapeutics (9th Ed) by J.G. Hardman, L.E. Limbird, P.B. Molinoff, R.W. Ruddon and A.G. Gilman (Editors) McGraw Hill, 1996. There are also texts that focus on the pharmacology of drugs for specific disease areas, or specific classes of drugs (e.g. natural products) or adverse drug interactions, among other subjects. Specific examples include:

The American Psychiatric Press Textbook of Psychopharmacology (2nd edition) by A.F. Schatzberg & C.B. Nemeroff (Editors), American Psychiatric Press, 1998; and Essential Psychopharmacology : Neuroscientific Basis and Practical Applications by N. Muntner and S.M. Stahl, Cambridge Univ Press, 1996.

There are also texts on pharmacogenetics which are particularly useful for identifying genes which may contribute to variable pharmacokinetic response. In addition there are texts on some of the major xenobiotic metabolizing proteins, such as the cytochrome P450 genes including Pharmacogenetics of Drug Metabolism (International Encyclopedia of Pharmacology and Therapeutics) by Werner Kalow (Editor) Pergamon Press, 1992; Genetic Factors in Drug Therapy : Clinical and Molecular Pharmacogenetics by D.A Price Evans, Cambridge Univ Press, 1993; Pharmacogenetics (Oxford Monographs on Medical Genetics, 32) by W.W. Weber, Oxford Univ Press, 1997; Cytochrome P450 : Structure, Mechanism, and Biochemistry by P.R. Ortiz de Montellano (Editor), Plenum Publishing Corp, 1995; and Appleton & Lange's Review of Pharmacy, 6th edition, (Appleton & Lange's Review Series) by G.D. Hall & B.S. Reiss, Appleton & Lange, 1997.

Genetics, Biochemistry and Molecular Biology Literature

In addition to the medical, pathology, and pharmacology texts listed above there are several information sources that one skilled in the art will turn to for information on the genetic, physiologic, biochemical, and molecular biological aspects of the disease, disorder or condition or the effect of the therapeutic intervention on specific physiologic processes. The biomedical literature may include information on nonhuman organisms that is relevant to understanding the likely disease or pharmacological pathways in man.

Also provided below are illustrative texts which will aid in the identification of a pathway or pathways, and a gene or genes that may be relevant to interindividual variation in response to a therapy. Textbooks of biochemistry, genetics and physiology are often useful sources for such pathway information. In order to ascertain the appropriate methods to analyze the effects of an allelic variance, variances, or haplotypes in vitro, one skilled in the art will review existing information on molecular biology, cell biology, genetics, biochemistry; and physiology. Such texts are useful sources for general and specific information on the genetic and biochemical processes involved in disease and in drug action, as well as experimental procedures that may be useful in performing in vitro research on an allelic variance, variances, or haplotye.

Texts on gene structure and function and RNA biochemistry will be useful in evaluating the consequences of variances that do not change the coding sequence

(silent variances). Such variances may alter the interaction of RNA with proteins or other regulatory molecules affecting RNA processing, polyadenylation, or export.

Molecular and Cellular Biology

Molecular Cell Biology by H. Lodish, D. Baltimore, A. Berk, L. Zipurksy & J. Darnell, W H Freeman & Co., 1995; Essentials of Molecular Biology, D. Freifelder and Malacinski, Jones and Bartlett, 1993; Genes and Genomes: A Changing Perspective, M. Singer and P. Berg, University Science Books, 1991; Gene Structure and Expression, J.D. Hawkins, 1996. Cambridge University Press; Molecular Biology of the Cell, 2nd edition, B. Alberts et al., Garland Publishing, 1994.

Molecular Genetics

The Metabolic and Molecular Bases of Inherited Disease by C. R. Scriver, A.L. Beaudet, W.S. Sly (Editors), 7th edition, McGraw Hill, 1995; Genetics and Molecular Biology, R. Schleif, 1994. 2nd edition, Johns Hopkins University Press; Genetics, P.J. Russell, 1996. 4th edition, Harper Collins; An Introduction to Genetic Analysis, Griffiths et al. 1993. 5th edition, W.H. Freeman and Company; Understanding Genetics: A molecular approach, Rothwell, 1993. Wiley-Liss

General Biochemistry

Biochemistry, L. Stryer, 1995. W.H. Freeman and Company; Biochemistry, D. Voet and J.G. Voet, 1995. John Wiley and Sons; Principles of Biochemistry, A.L. Lehninger, D.L. Nelson, and M.M. Cox, 1993. Worth Publishers; Biochemistry, G. Zubay, 1998. Wm. C. Brown Communications; Biochemistry, C.K. Mathews and K.E. van Holde, 1990. Benjamin/Cummings

Transcription

Eukaryotic Transcription Factors, D.S. Latchman, 1995. Academic Press; Eukaryotic Gene Transcription, S. Goodbourn (ed.), 1996. Oxford University Press; Transcription Factors and DNA Replication, D.S. Pederson and N.H. Heintz, 1994. CRC Press/R.G. Landes Company; Transcriptional Regulation, S.L. McKnight and K. Yamamoto (eds.), 1992. 2 volumes, Cold Spring Harbor Laboratory Press

RNA

Control of Messenger RNA Stability, J. Belasco and G. Brawerman (eds.), 1993. Academic Press; RNA-Protein Interactions, Nagai and Mattaj (eds.), 1994. Oxford

University Press; mRNA Metabolism and Post-transcriptional Gene Regulation, Harford and Morris (eds.), 1997. Wiley-Liss.

Translation

- 5 Translational Control, J.W.B. Hershey, M.B. Mathews, and N. Sonenberg (eds.), 1995. Cold Spring Harbor Laboratory Press

General Physiology

- 10 Textbook of Medical Physiology 9th Edition by A.C. Guyton and J.E. Hall W.B. Saunders, 1997; Review of Medical Physiology, 18th Edition by W.F. Ganong, Appleton and Lange, 1997.

Online Databases

- ... Those skilled in the art are familiar with how to search the biomedical literature, such as, e.g., libraries, online PubMed, abstract listings, and online
15 mutation databases. One particularly useful resource is maintained at the web site of the National Center for Biotechnology Information (ncbi):
<http://www.ncbi.nlm.nih.gov/>. From the ncbi site one can access Online Mendelian Inheritance in Man (OMIM),. OMIM can be found at:
<http://www3.ncbi.nlm.nih.gov/Omim/searchomim.html>. OMIM is a medically
20 oriented database of genetic information with entries for thousands of genes. The OMIM record number is provided for many of the genes in Tables 1-6 and 12-23 (see column 3), and constitutes an excellent entry point for identification of references that point to the broader literature. Another useful site at NCBI is the Entrez browser, located at <http://www3.ncbi.nlm.nih.gov/Entrez/>. One can search
25 genomes, polynucleotides, proteins, 3D structures, taxonomy or the biomedical literature (PubMed) via the Entrez site. More generally links to a number of useful sites with biomedical or genetic data are maintained at sites such as Med Web at the Emory University Health Sciences Center Library:
<http://WWW.MedWeb.Emory.Edu/MedWeb/>; Riken, a Japanese web site at:
30 <http://www.rtc.riken.go.jp/othersite.html> with links to DNA sequence, structural, molecular biology, bioinformatics, and other databases; at the Oak Ridge National Laboratory web site: <http://www.ornl.gov/hgmis/links.html>; or at the Yahoo website of Diseases and Conditions:
http://dir.yahoo.com/health/diseases_and_conditions/index.html. Each of the
35 indicated web sites has additional useful links to other sites.

Another type of database with utility in selecting the genes on a biochemical pathway that may affect the response to a drug are databases that provide information on biochemical pathways. Examples of such databases include the Kyoto Encyclopedia of Genes and Genomes (KEGG), which can be found at:

5 <http://www.genome.ad.jp/kegg/kegg.html>. This site has pictures of many biochemical pathways, as well as links to other metabolic databases such as the well known Boehringer Mannheim biochemical pathways charts:

<http://www.expasy.ch/cgi-bin/search-biochem-index>. The metabolic charts at the latter site are comprehensive, and excellent starting points for working out the salient enzymes on any given pathway.

Each of the web sites mentioned above has links to other useful web sites, which in turn can lead to additional sites with useful information. *Research Libraries*

Those skilled in the art will often require information found only at large libraries. The National Library of Medicine (<http://www.nlm.nih.gov/>) is the largest medical library in the world and its catalogs can be searched online. Other libraries, such as university or medical school libraries are also useful to conduct searches. Biomedical books such as those referred to above can often be obtained from online bookstores as described above.

Biomedical Literature

20 To obtain up to date information on drugs and their mechanism of action and biotransformation; disease pathophysiology; biochemical pathways relevant to drug action and disease pathophysiology; and genes that encode proteins relevant to drug action and disease one skilled in the art will consult the biomedical literature. A widely used, publically accessible web site for searching published journal articles is PubMed (<http://www.ncbi.nlm.nih.gov/PubMed/>). At this site, one can search for the most recent articles (within the last 1-2 months) or older literature (back to 1966). Many Journals also have their own sites on the world wide web and can be searched online. For example see the IDEAL web site at:

25 <http://www.apnet.com/www/ap/aboutid.html>. This site is an online library, featuring full text journals from Academic Press and selected journals from W.B. Saunders and Churchill Livingstone. The site provides access (for a fee) to nearly 2000 scientific, technical, and medical journals.

Experimental methods for identification of genes involved in the action of a drug

There are a number of experimental methods for identifying genes and gene products that mediate or modulate the effects of a drug or other treatment. They encompass analyses of RNA and protein expression as well as methods for detecting protein – protein interactions and protein – ligand interactions. Two preferred ,
5 experimental methods for identification of genes that may be involved in the action of a drug are (1) methods for measuring the expression levels of many mRNA transcripts in cells or organisms treated with the drug (2) methods for measuring the expression levels of many proteins in cells or organisms treated with the drug.

RNA transcripts or proteins that are substantially increased or decreased in
10 drug treated cells or tissues relative to control cells or tissues are candidates for mediating the action of the drug. Preferably the level of an mRNA is at least 30% higher or lower in drug treated cells, more preferably at least 50% higher or lower, and most preferably two fold higher or lower than levels in non-drug treated control cells. The analysis of RNA levels can be performed on total RNA or on
15 polyadenylated RNA selected by oligodT affinity. Further, RNA from different cell compartments can be analyzed independently – for example nuclear vs. cytoplasmic RNA. In addition to RNA levels, RNA kinetics can be examined, or the pool of RNAs currently being translated can be analyzed by isolation of RNA from polysomes. Other useful experimental methods include protein interaction methods
20 such as the yeast two hybrid system and variants thereof which facilitate the detection of protein – protein interactions. Preferably one of the interacting proteins is the drug target or another protein strongly implicated in the action of the compound being assessed.

The pool of RNAs expressed in a cell is sometimes referred to as the
25 transcriptome. Methods for measuring the transcriptome, or some part of it, are known in the art. A recent collection of articles summarizing some current methods appeared as a supplement to the journal *Nature Genetics*. (The Chipping Forecast. *Nature Genetics* supplement, volume 21, January 1999.) A preferred method for measuring expression levels of mRNAs is to spot PCR products corresponding to a
30 large number of specific genes on a nylon membrane such as Hybond N Plus (Amersham-Pharmacia). Total cellular mRNA is then isolated, labelled by random oligonucleotide priming in the presence of a detectable label (e.g. alpha 33P labelled radionucleotides or dye labelled nucleotides), and hybridized with the filter containing the PCR products. The resulting signals can be analyzed by
35 commercially available software, such as can be obtained from Clontech/Molecular Dynamics or Research Genetics, Inc.

Experiments have been described in model systems that demonstrate the utility of measuring changes in the transcriptome before and after changing the growth conditions of cells, for example by changing the nutrient environment. The changes in gene expression help reveal the network of genes that mediate physiological responses to the altered growth condition. Similarly, the addition of a drug to the cellular or in vivo environment, followed by monitoring the changes in gene expression can aid in identification of gene networks that mediate pharmacological responses.

The pool of proteins expressed in a cell is sometimes referred to as the proteome. Studies of the proteome may include not only protein abundance but also protein subcellular localization and protein-protein interaction. Methods for measuring the proteome, or some part of it, are known in the art. One widely used method is to extract total cellular protein and separate it in two dimensions, for example first by size and then by isoelectric point. The resulting protein spots can be stained and quantitated, and individual spots can be excised and analyzed by mass spectrometry to provide definitive identification. The results can be compared from two or more cell lines or tissues, at least one of which has been treated with a drug. The differential up or down modulation of specific proteins in response to drug treatment may indicate their role in mediating the pharmacologic actions of the drug. Another way to identify the network of proteins that mediate the actions of a drug is to exploit methods for identifying interacting proteins. By starting with a protein known to be involved in the action of a drug – for example the drug target – one can use systems such as the yeast two hybrid system and variants thereof (known to those skilled in the art; see Ausubel et al., *Current Protocols in Molecular Biology*, op. cit.) to identify additional proteins in the network of proteins that mediate drug action. The genes encoding such proteins would be useful for screening for DNA sequence variances, which in turn may be useful for analysis of interpatient variation in response to treatments. For example, the protein 5-lipoxygenase (5LO) is an enzyme which is at the beginning of the leukotriene biosynthetic pathway and is a target for anti-inflammatory drugs used to treat asthma and other diseases. In order to detect proteins that interact with 5-lipoxygenase the two-hybrid system was recently used to isolate three different proteins, none previously known to interact with 5LO. (Provost et al., *Interaction of 5-lipoxygenase with cellular proteins. Proc. Natl. Acad. Sci. U.S.A.* 96: 1881-1885, 1999.) A recent collection of articles summarizing some current methods in proteomics appeared in the August 1998 issue of the journal *Electrophoresis* (volume 19, number 11). Other useful articles include: Blackstock WP, et al.

Proteomics: quantitative and physical mapping of cellular proteins. *Trends Biotechnol.* 17 (3): p. 121-7, 1999, and Patton W.F., Proteome analysis II. Protein subcellular redistribution: linking physiology to genomics via the proteome and separation technologies involved. *J Chromatogr B Biomed Sci App.* 722(1-2):203-23. 1999.

Since many of these methods can also be used to assess whether specific polymorphisms are likely to have biological effects, they are also relevant in section 3, below, concerning methods for assessing the likely contribution of variances in candidate genes to clinical variation in patient responses to therapy.

2. Screen for Variances in Genes that may be Related to Therapeutic Response

Having identified a set of genes that may affect response to a drug the next step is to screen the genes for variances that may account for interindividual variation in response to the drug. There are a variety of levels at which a gene can be screened for variances, and a variety of methods for variance screening. The two main levels of variance screening are genomic DNA screening and cDNA screening. Genomic variance detection may include screening the entire genomic segment spanning the gene from 2 kb to 10 kb upstream of the transcription start site to the polyadenylation site, or 2 to 10 kb beyond the polyadenylation site. Alternatively genomic variance detection may (for intron containing genes) include the exons and some region around them containing the splicing signals, for example, but not all of the intronic sequences. In addition to screening introns and exons for variances it is generally desirable to screen regulatory DNA sequences for variances. Promoter, enhancer, silencer and other regulatory elements have been described in human genes. The promoter is generally proximal to the transcription start site, although there may be several promoters and several transcription start sites. Enhancer, silencer and other regulatory elements may be intragenic or may lie outside the introns and exons, possibly at a considerable distance, such as 100 kb away. Variances in such sequences may affect basal gene expression or regulation of gene expression. In either case such variation may affect the response of an individual patient to a therapeutic intervention, for example a drug, as described in the examples. Thus in practicing the present invention it is useful to screen regulatory sequences as well as transcribed sequences, in order to identify variances that may affect gene transcription. Frequently the genomic sequence of a gene can be found in the sources above, particularly by searching GenBank or Medline (PubMed). The name of the gene can be entered at a site such as Entrez: <http://www.ncbi.nlm.nih.gov/Entrez/nucleotide.html>. Using the genomic sequence

and information from the biomedical literature one skilled in the art can perform a variance detection procedure such as those described in examples 2, 3, 4.

Variance detection is often first performed on the cDNA of a gene for several reasons. First, available data on functional sequence variances suggests that
5 variances in the transcribed portion of a gene may be most likely to have functional consequences as they can affect the interaction of the transcript with a wide variety of cellular factors during the complex processes of RNA transcription, processing and translation, with consequent effects on RNA splicing, stability, translational efficiency or other processes. Second, as a practical matter the cDNA sequence of a
10 gene is often available before the genomic structure is known, although the reverse will be true in the future as the sequence of the human genome is determined. Third, the cDNA is often compact compared to the genomic locus, and can be screened for variances with much less effort. If the genomic structure is not known then only the cDNA sequence can be scanned for variances. Methods for preparing cDNA are
15 described in Example 1. Methods for variance detection on cDNA are described below and in the examples.

In general it is preferable to catalog genetic variation at the genomic DNA level because there are an increasing number of well documented instances of functionally important variances that lie outside of transcribed sequence. Also, to
20 properly use optimal genetic methods to assess the contribution of a candidate gene to variation in a phenotype of interest it is desirable to understand the character of sequence variation in the candidate gene: what is the nature of linkage disequilibrium between different variances in the gene; are there sites of recombination within the gene; what is the extent of homoplasy in the gene (i.e.
25 occurrence of two variant sites that are identical by state but not identical by descent because the same variance arose at least twice in human evolutionary history on two different haplotypes); what are the different haplotypes and how can they be grouped to increase the power of genetic analysis?

Methods for variance screening have been described, including DNA
30 sequencing. See for example: US5698400: Detection of mutation by resolvase cleavage; US5217863: Detection of mutations in nucleic acids; and US5750335: Screening for genetic variation, as well as the examples and references cited therein for examples of useful variance detection procedures. Detailed variance detection procedures are also described in examples 2, 3, 4. One skilled in the art will
35 recognize that depending on the specific aims of a variance detection project (number of genes being screened, number of individuals being screened, total length

of DNA being screened) one of the above cited methods may be preferable to the others, or yet another procedure may be optimal. A preferred method of variance detection is chain terminating DNA sequencing using dye labeled primers, cycle sequencing and software for assessing the quality of the DNA sequence as well as specialized software for calling heterozygotes. The use of such procedures has been described by Nickerson and colleagues. See for example: Rieder M.J., et al. Automating the identification of DNA variations using quality-based fluorescence re-sequencing: analysis of the human mitochondrial genome. *Nucleic Acids Res.* 26 (4):967-73, 1998, and: Nickerson D.A., et al. PolyPhred: automating the detection and genotyping of single nucleotide substitutions using fluorescence-based resequencing. *Nucleic Acids Res.* 25 (14):2745-51, 1997. Although the variances provided in Tables 12-17, and 18-23 consist principally of cDNA variances, it is an aspect of this invention that detection of genomic variances is also a useful method for identification of variances that may account for interpatient variation in response to a therapy.

Another important aspect of variance detection is the use of DNA from a panel of human subjects that represents a known population. For example, if the subjects are being screened for variances relevant to a specific drug development program it is desirable to include both subjects with the target disease and healthy subjects in the panel, because certain variances may occur at different frequencies in the healthy and disease populations and can only be reliably detected by screening both populations. Also, for example, if the drug development program is taking place in Japan, it is important to include Japanese individuals in the screening population. In general, it is always desirable to include subjects of known geographic, racial or ethnic identity in a variance screening experiment so the results can be interpreted appropriately for different patient populations, if necessary. Also, in order to select optimal sets of variances for genetic analysis of a gene locus it is desirable to know which variances have occurred recently – perhaps on multiple different chromosomes - and which are ancient. Inclusion of one or more apes or monkeys in the variance screening panel is one way of gaining insight into the evolutionary history of variances. Chimpanzees are preferred subjects for inclusion in a variance screening panel.

3. Assess the Likely Contribution of Variances in Candidate Genes to Clinical Variation in Patient Responses to Therapy

Once a set of genes likely to affect disease pathophysiology or drug action has been identified, and those genes have been screened for variances, said variances

(e.g., provided in Tables 12-17, and 18-23) can be assessed for their contribution to variation in the pharmacological or toxicological phenotypes of interest. Such studies are useful for reducing a large number of candidate variances to a smaller number of variances to be tested in clinical trials. There are several methods which can be used in the present invention for assessing the medical and pharmaceutical implications of a DNA sequence variance. They range from computational methods to *in vitro* and/or *in vivo* experimental methods, to prospective human clinical trials, and also include a variety of other laboratory and clinical measures that can provide evidence of the medical consequences of a variance. In general, human clinical trials constitute the highest standard of proof that a variance or set of variances is useful for selecting a method of treatment, however, computational and *in vitro* data, or retrospective analysis of human clinical data may provide strong evidence that a particular variance will affect response to a given therapy, often at lower cost and in less time than a prospective clinical trial. Moreover, at an early stage in the analysis when there are many possible hypotheses to explain interpatient variation in treatment response, the use of informatics-based approaches to evaluate the likely functional effects of specific variances is an efficient way to proceed.

Informatics-based approaches to the prediction of the likely functional effects of variances include DNA and protein sequence analysis (phylogenetic approaches and motif searching) and protein modeling (based on coordinates in the protein database, or pdb; see <http://www.rcsb.org/pdb/>). See, for example: Kawabata et al. The Protein Mutant Database. *Nucleic Acids Research* 27: 355-357, 1999; also available at: <http://pmd.ddbj.nig.ac.jp>. Such analyses can be performed quickly and inexpensively, and the results may allow selection of certain genes for more extensive *in vitro* or *in vivo* studies or for more variance detection or both.

The three dimensional structure of many medically and pharmaceutically important proteins, or homologs of such proteins in other species, or examples of domains present in such proteins, is known as a result of x-ray crystallography studies and, increasingly, nuclear magnetic resonance studies. Further, there are increasingly powerful tools for modeling the structure of proteins with unsolved structure, particularly if there is a related (homologous) protein with known structure. (For reviews see: Rost et al., Protein fold recognition by prediction-based threading, *J. Mol. Biol.* 270:471-480, 1997; Firestine et al., Threading your way to protein function, *Chem. Biol.* 3:779-783, 1996) There are also powerful methods for identifying conserved domains and vital amino acid residues of proteins of unknown structure by analysis of phylogenetic relationships. (Deleage et al., Protein structure prediction: Implications for the biologist, *Biochimie* 79:681-686, 1997; Taylor et al., Multiple protein structure alignment, *Protein Sci.* 3:1858-1870, 1994) These

methods can permit the prediction of functionally important variances, either on the basis of structure or evolutionary conservation. For example, a crystal structure can reveal which amino acids comprise a small molecule binding site. The identification of a polymorphic amino acid variance in the topological neighborhood of such a site, and, in particular, the demonstration that at least one variant form of the protein has a variant amino acid which impinges on (or which may otherwise affect the chemical environment around) the small molecule binding pocket differently from another variant form, provides strong evidence that the variance may affect the function of the protein. From this it follows that the interaction of the protein with a treatment method, such as an administered compound, will likely be variable between different patients. One skilled in the art will recognize that the application of computational tools to the identification of functionally consequential variances involves applying the knowledge and tools of medicinal chemistry and physiology to the analysis.

Phylogenetic approaches to understanding sequence variation are also useful. Thus if a sequence variance occurs at a nucleotide or encoded amino acid residue where there is usually little or no variation in homologs of the protein of interest from non-human species, particularly evolutionarily remote species, then the variance is more likely to affect function of the RNA or protein. Computational methods for phylogenetic analysis are known in the art, (see below for citations of some methods).

Computational methods are also useful for analyzing DNA polymorphisms in transcriptional regulatory sequences, including promoters and enhancers. One useful approach is to compare variances in potential or proven transcriptional regulatory sequences to a catalog of all known transcriptional regulatory sequences, including consensus binding domains for all transcription factor binding domains. See, for example, the databases cited in: Burks, C. *Molecular Biology Database List. Nucleic Acids Research* 27: 1-9, 1999, and links to useful databases on the internet at:

http://www.oup.co.uk/nar/Volume_27/issue_01/summary/gkc105_gml.html. In particular see the Transcription Factor Database (Heinemeyer, T., et al. (1999) Expanding the TRANSFAC database towards an expert system of regulatory molecular mechanisms. *Nucleic Acids Res.* 27: 318-322, or on the internet at: <http://193.175.244.40/TRANSFAC/index.html>). Any sequence variances in transcriptional regulatory sequences can be assessed for their effects on mRNA levels using standard methods, either by making plasmid constructs with the different allelic forms of the sequence, transfecting them into cells and measuring the output of a reporter transcript, or by assays of cells with different endogenous

alleles of variances. One example of a polymorphism in a transcriptional regulatory element that has a pharmacogenetic effect is described by Drazen et al. (1999) Pharmacogenetic association between ALOX5 promoter genotype and the response to anti-asthma treatment. *Nature Genetics* 22: 168-170. Drazen and co-workers
5 found that a polymorphism in an Sp1-transcription factor binding domain, which varied among subjects from 3-6 tandem copies, accounted for varied expression levels of the 5-lipoxygenase gene when assayed in vitro in reporter construct assays. This effect would have been flagged by an informatics analysis that surveyed the 5-lipoxygenase candidate promoter region for transcriptional regulatory sequences
10 (resulting in discovery of polymorphism in the Sp1 motif).

4. Perform *in vitro* or *in vivo* Experiments to Assess the Functional Importance of Gene Variances

There are two broad types of studies useful for assessing the likely
15 importance of variances: analysis of RNA or protein abundance (as described above in the context of methods for identifying candidate genes for explaining interpatient variation in treatment response) or analysis of functional differences in different variant forms of a gene, mRNA or protein. Studies of functional differences may involve direct measurements of biochemical activity of different variant forms of an
20 mRNA or protein, or may involve assaying the influence of a variance or variances on various cell properties, including both tissue culture and *in vivo* studies.

The selection of an appropriate experimental program for testing the medical consequences of a variance may differ depending on the nature of the variance, the gene, and the disease. For example if there is already evidence that a protein is
25 involved in the pharmacologic action of a drug, then the *in vitro* or *in vivo* demonstration that an amino acid variance in the protein affects its biochemical activity is strong evidence that the variance will have an effect on the pharmacology of the drug in patients, and therefore that patients with different variant forms of the gene may have different responses to the same dose of drug. If the variance is silent
30 with respect to protein coding information, or if it lies in a noncoding portion of the gene (e.g., a promoter, an intron, or a 5'- or 3'-untranslated region) then the appropriate biochemical assay may be to assess mRNA abundance, half life, or translational efficiency. If, on the other hand, there is no substantial evidence that the protein encoded by a particular gene is relevant to drug pharmacology, but
35 instead is a candidate gene on account of its involvement in disease pathophysiology, then the optimal test may be a clinical study addressing whether two patient groups distinguished on the basis of the variance respond differently to a therapeutic intervention. This approach reflects the current reality that biologists do

not sufficiently understand gene regulation, gene expression and gene function to consistently make accurate inferences about the consequences of DNA sequence variances for pharmacological responses.

In summary, if there is a plausible hypothesis regarding the effect of a protein on the action of a drug, then *in vitro* and *in vivo* approaches, including those described below, will be useful to predict whether a given variance is therapeutically consequential. If, on the other hand, there is no evidence of such an effect, then the preferred test is an empirical clinical measure of the impact to the variance on efficacy or toxicity *in vivo* (which requires no evidence or assumptions regarding the mechanism by which the variance may exert an effect on a therapeutic response). However, given the expense and statistical constraints of clinical trials, it is preferable to limit clinical testing to variances for which there is at least some experimental or computational evidence of a functional effect.

Experimental Methods: Genomic DNA Analysis

Variances in DNA may affect the basal transcription or regulated transcription of a gene locus. Such variances may be located in any part of the gene but are most likely to be located in the promoter region, the first intron, or in 5' or 3' flanking DNA, where enhancer or silencer elements may be located. Methods for analyzing transcription are well known to those skilled in the art and exemplary methods are briefly described above and in some of the texts cited elsewhere in this application. Transcriptional run off assay is one useful method. Detailed protocols can be found in texts such as: Current Protocols in Molecular Biology edited by: F.M. Ausubel, et al. John Wiley & Sons, Inc, 1999, or: Molecular Cloning: A Laboratory Manual by J. Sambrook, E.F. Fritsch and T Maniatis. 1989. 3 vols, 2nd edition, Cold Spring Harbor Laboratory Press

Experimental Methods: RNA Analysis

RNA variances may affect a wide range of processes including RNA splicing, polyadenylation, capping, export from the nucleus, interaction with translation initiation, elongation or termination factors, or the ribosome, or interaction with cellular factors including regulatory proteins, or factors that may affect mRNA half life. However, the effect of most RNA sequence variances on RNA function, if any, should ultimately be measurable as an effect on RNA or protein levels – either basal levels or regulated levels or levels in some abnormal cell state, such as cells from patients with a disease. Therefore, one preferred method for assessing the effect of RNA variances on RNA function is to measure the levels of RNA produced by different alleles in one or more conditions of cell or tissue

growth. Said measuring can be done by conventional methods such as Northern blots or RNAase protection assays (kits available from Ambion, Inc.), or by methods such as the Taqman assay (developed by the Applied Biosystems Division of the Perkin Elmer Corporation), or by using arrays of oligonucleotides or arrays of cDNAs attached to solid surfaces. Systems for arraying cDNAs are available commercially from companies such as Nanogen and General Scanning. Complete systems for gene expression analysis are available from companies such as Molecular Dynamics. For recent reviews of systems for high throughput RNA expression analysis see the supplement to volume 21 of Nature Genetics entitled "The Chipping Forecast", especially articles beginning on pages 9, 15, 20 and 25.

Additional methods for analyzing the effect of variances on RNA include secondary structure probing, and direct measurement of half life or turnover. Secondary structure can be determined by techniques such as enzymatic probing (using enzymes such as T1, T2 and S1 nuclease), chemical probing or RNAase H probing using oligonucleotides. Most RNA structural assays are performed *in vitro*, however some techniques can be performed on cell extracts or even in living cells, using fluorescence resonance energy transfer to monitor the state of RNA probe molecules.

Experimental Methods: Protein Analysis

There are a variety of experimental methods for investigating the effect of an amino acid variance on response of a patient to a treatment. The preferred method will depend on the availability of cells expressing a particular protein, and the feasibility of a cell-based assay vs. assays on cell extracts, on proteins produced in a foreign host, or on proteins prepared by *in vitro* translation.

For example, the methods and systems listed below can be utilized to demonstrate differential expression, stability and/or activity of different variant forms of a protein, or in phenotype/genotype correlations in a model system.

For the determination of protein levels or protein activity a variety of techniques are available. The *in vitro* protein activity can be determined by transcription or translation in bacteria, yeast, baculovirus, COS cells (transient), Chinese Hamster Ovary (CHO) cells, or studied directly in human cells, or other cell systems can be used. Further, one can perform pulse chase experiments to determine if there are changes in protein stability (half-life).

One skilled in the art can construct cell based assays of protein function, and then perform the assays in cells with different genotypes or haplotypes. For example, identification of cells with different genotypes, e.g. cell lines established from families and subsequent determination of relevant protein phenotypes (e.g.

expression levels, post translational modifications, activity assays) may be performed using standard methods.

Assays of protein levels or function can also be performed on cell lines (or extracts from cell lines) derived from pedigrees in order to determine whether there is a genetic component to variation in protein levels or function. The experimental analysis is as above for RNAs, except the assays are different. Experiments can be performed on naive cells or on cells subjected to various treatments, including pharmacological treatments.

In another approach to the study of amino acid variances one can express genes corresponding to different alleles in experimental organisms and examine effects on disease phenotype (if relevant in the animal model), or on response to the presence of a compound. Such experiments may be performed in animals that have disrupted copies of the homologous gene (e.g. gene knockout animals engineered to be deficient in a target gene), or variant forms of the human gene may be introduced into germ cells by transgenic methods, or a combination of approaches may be used. To create animal strains with targeted gene disruptions a DNA construct is created (using DNA sequence information from the host animal) that will undergo homologous recombination when inserted into the nucleus of an embryonic stem cell. The targeted gene is effectively inactivated due to the insertion of non-natural sequence – for example a translation stop codon or a marker gene sequence that interrupts the reading frame. Well known PCR based methods are then used to screen for those cells in which the desired homologous recombination event has occurred. Gene knockouts can be accomplished in worms, drosophila, mice or other organisms. Once the knockout cells are created (in whatever species) the candidate therapeutic intervention can be administered to the animal and pharmacological or biological responses measured, including gene expression levels. If variant forms of the gene are useful in explaining interpatient variation in response to the compound in man, then complete absence of the gene in an experimental organism should have a major effect on drug response. As a next step various human forms of the gene can be introduced into the knockout organism (a technique sometimes referred to as a knock-in). Again, pharmacological studies can be performed to assess the impact of different human variances on drug response. Methods relevant to the experimental approaches described above can be found in the following exemplary texts:

General Molecular Biology Methods

Molecular Biology: A project approach, S.J. Karcher, Fall 1995. Academic Press; DNA Cloning: A Practical Approach, D.M. Glover and B.D. Hayes (eds). 1995. IRL/Oxford University Press. Vol. 1 - Core Techniques; Vol 2 - Expression Systems; Vol. 3 -

Complex Genomes; Vol. 4 -Mammalian Systems; Short Protocols in Molecular Biology, Ausubel et al. October 1995. 3rd edition, John Wiley and Sons; Current Protocols in Molecular Biology Edited by: F.M. Ausubel, R.Brent, R.E. Kingston, D.D. Moore, J.G. Seidman, K. Struhl, (Series Editor: V.B. Chanda), 1988; Molecular Cloning: A laboratory manual, J. Sambrook, E.F. Fritsch. 1989. 3 vols, 2nd edition, Cold Spring Harbor Laboratory Press.

Polymerase chain reaction (PCR)

PCR Primer: A laboratory manual, C.W. Diffenbach and G.S. Dveksler (eds.). 1995. Cold Spring Harbor Laboratory Press; The Polymerase Chain Reaction, K.B. Mullis et al. (eds.), 1994. Birkhauser; PCR Strategies, M.A. Innis, D.H. Gelf, and J.J. Sninsky (eds.), 1995. Academic Press.

General procedures for discipline specific studies

Current Protocols in Neuroscience Edited by: J. Crawley, C. Gerfen, R. McKay, M. Rogawski, D. Sibley, P. Skolnick, (Series Editor: G. Taylor), 1997; Current Protocols in Pharmacology Edited by: S. J. Enna / M. Williams, J.W. Ferkany, T. Kenakin, R.E. Porsolt, J.P. Sullivan, (Series Editor: G. Taylor), 1998; Current Protocols in Protein Science Edited by: J.E. Coligan, B.M. Dunn, H.L. Ploegh, D.W. Speicher, P.T. Wingfield, (Series Editor: Virginia Benson Chanda), 1995; Current Protocols in Cell Biology Edited by: J.S. Bonifacino, M. Dasso, J. Lippincott-Schwartz, J.B. Harford, K.M. Yamada, (Series Editor: K. Morgan) 1999; Current Protocols in Cytometry Managing Editor: J.P. Robinson, Z. Darzynkiewicz (ed) / P. Dean (ed), A. Orfao (ed), P. Rabinovitch (ed), C. Stewart (ed), H. Tanke (ed), L. Wheelless (ed), (Series Editor: J. Paul Robinson), 1997; Current Protocols in Human Genetics Edited by: N.C. Dracopoli, J.L. Haines, B.R. Korf, et al., (Series Editor: A. Boyle), 1994; Current Protocols in Immunology Edited by: J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W. Strober, (Series Editor: R. Coico), 1991.

IV. Clinical Trials

A clinical trial is the definitive test of the utility of a variance or variances for the selection of optimal therapy. A clinical trial in which an interaction of gene variances and clinical outcomes (desired or undesired) is explored will be referred to herein as a "pharmacogenetic clinical trial". Pharmacogenetic clinical trials require no knowledge of the biological function of the gene containing the variance or variances to be assessed, nor any knowledge of how the therapeutic intervention to be assessed works at a biochemical level. The pharmacogenetics effects of a variance can be addressed at a purely statistical level: either a particular variance or

set of variances is consistently associated with a significant difference in a salient drug response parameter (e.g. response rate, effective dose, side effect rate, etc.) or not. On the other hand, if there is information about either the biochemical basis of a therapeutic intervention or the biochemical effects of a variance, then a
5 pharmacogenetic clinical trial can be designed to test a specific hypothesis. In preferred embodiments of the methods of this application the mechanism of action of the compound to be genetically analyzed is at least partially understood.

Methods for performing clinical trials are well known in the art. (see e.g. Guide to Clinical Trials by Bert Spilker, Raven Press, 1991; The Randomized
10 Clinical Trial and Therapeutic Decisions by Niels Tygstrup (Editor), Marcel Dekker; Recent Advances in Clinical Trial Design and Analysis (Cancer Treatment and Research, Ctar 75) by Peter F. Thall (Editor) Kluwer Academic Pub, 1995. Clinical Trials: A Methodologic Perspective by Steven Piantadosi, Wiley Series in
15 Probability and Statistics, 1997). However, performing a clinical trial to test the genetic contribution to interpatient variation in drug response entails additional design considerations, including (i) defining the genetic hypothesis or hypotheses, (ii) devising an analytical strategy for testing the hypothesis, including
determination of how many patients will need to be enrolled to have adequate statistical power to measure an effect of a specified magnitude (power analysis), (iii)
20 definition of any primary or secondary genetic endpoints, and (iv) definition of methods of statistical genetic analysis, as well as other aspects. In the outline below some of the major types of genetic hypothesis testing, power analysis and statistical testing and their application in different stages of the drug development process are reviewed. One skilled in the art will recognize that certain of the methods will be
25 best suited to specific clinical situations, and that additional methods are known and can be used in particular instances.

A. *Performing a Clinical Trial: Overview*

As used herein, a "clinical trial" is the testing of a therapeutic intervention in
30 a volunteer human population for the purpose of determining whether it is safe and/or efficacious in the treatment of a disease, disorder, or condition. The present invention describes methods for achieving superior efficacy and/or safety in a genetically defined subgroup defined by the presence or absence of at least one gene sequence variance, compared to the effect that could be obtained in a conventional
35 trial (without genetic stratification).

A "clinical study" is that part of a clinical trial that involves determination of the effect of a candidate therapeutic intervention on human subjects. It includes clinical evaluation of physiologic responses including pharmacokinetic (bioavailability as affected by drug absorption, distribution, metabolism and excretion) and pharmacodynamic (physiologic response and efficacy) parameters. A pharmacogenetic clinical study (or clinical trial) is a clinical study that involves testing of one or more specific hypotheses regarding the interaction of a genetic variance or variances (or set of variances, i.e. haplotype or haplotypes) on response to a therapeutic intervention. Pharmacogenetic hypotheses are formulated before the study, and may be articulated in the study protocol in the form of primary or secondary endpoints. For example an endpoint may be that in a particular genetic subgroup the rate of objectively defined responses exceeds the response rate in a control group (either the entire control group or the subgroup of controls with the same genetic signature as the treatment subgroup they are being compared to) or exceeds that in the whole treatment group (i.e. without genetic stratification) by some predefined relative or absolute amount.

For a clinical study to commence enrollment and proceed to treat subjects at an institution that receives any federal support (most medical institutions in the US), an application that describes in detail the scientific premise for the therapeutic intervention and the procedures involved in the study, including the endpoints and analytical methods to be used in evaluating the data, must be reviewed and accepted by a review panel, often termed an Institutional Review Board (IRB). Similarly any clinical study that will ultimately be evaluated by the FDA as part of a new drug or product application (or other application as described below), must be reviewed and approved by an IRB. The IRB is responsible for determining that the trial protocol is safe, conforms to established ethical principles and guidelines, has risks proportional to any expected benefits, assures equitable selection of patients, provides sufficient information to patients (via a consent form) to insure that they can make an informed decision about participation, and insures the privacy of participants and the confidentiality of any data collected. (See the report of the National Commission for Protection of Human Subjects of Biomedical and Behavioral Research (1978). The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research. Washington, D.C.: DHEW Publication Number (OS) 78-0012. For a recent review see: Coughlin, S.S. (ed.) (1995) Ethics in Epidemiology and Clinical Research. Epidemiology Resources, Newton, MA.) The European counterpart of the US FDA is the European Medicines Evaluation Agency (EMA). Similar agencies exist in other

countries and are responsible for insuring, via the regulatory process, that clinical trials conform to similar standards as are required in the US. The documents reviewed by an IRB include a clinical protocol containing the information described above, and a consent form.

5 It is also customary, but not required, to prepare an investigator's brochure which describes the scientific hypothesis for the proposed therapeutic intervention, the preclinical data, and the clinical protocol. The brochure is made available to any physician participating in the proposed or ongoing trial.

10 The supporting preclinical data is a report of all the *in vitro*, *in vivo* animal or previous human trial or other data that supports the safety and/or efficacy of a given therapeutic intervention. In a pharmacogenetic clinical trial the preclinical data may also include a description of the effect of a specific genetic variance or variances on biochemical or physiologic experimental variables *in vitro* or *in vivo*, or on treatment outcomes, as determined by *in vivo* studies in animals or humans (for example in an
15 earlier trial), or by retrospective genetic analysis of clinical trial or other medical data (see below) used to formulate or strengthen a pharmacogenetic hypothesis. For example, case reports of unusual pharmacological responses in individuals with rare alleles (e.g. mutant alleles), or the observation of clustering of pharmacological responses in family members may provide the rationale for a pharmacogenetic
20 clinical trial.

The clinical protocol provides the relevant scientific and therapeutic introductory information, describes the inclusion and exclusion criteria for human subject enrollment, including genetic criteria if relevant (e.g. if genotype is to be among the enrollment criteria), describes in detail the exact procedure or procedures
25 for treatment using the candidate therapeutic intervention, describes laboratory analyses to be performed during the study period, and further describes the risks (both known and possible) involving the use of the experimental candidate therapeutic intervention. In a clinical protocol for a pharmacogenetic clinical trial, the clinical protocol will further describe the genetic variance and/or variances
30 hypothesized to account for differential responses in the normal human subjects or patients and supporting preclinical data, if any, a description of the methods for genotyping, genetic data collection and data handling as well as a description of the genetic statistical analysis to be performed to measure the interaction of the variance or variances with treatment response. Further, the clinical protocol for a
35 pharmacogenetic clinical trial will include a description of the genetic study design. For example patients may be stratified by genotype and the response rates in the different groups compared, or patients may be segregated by response and the genotype frequencies in the different responder or nonresponder groups measured.

One or more gene sequence variances or a combination of variances and/or haplotypes may be studied.

The informed consent document is a description of the therapeutic intervention and the clinical protocol in simple language (e.g. third grade level) for the patient to read, understand, and, if willing, agree to participate in the study by signing the document. In a pharmacogenetic clinical study the informed consent document will describe, in simple language, the use of a genetic test or a limited set of genetic tests to determine the subject or patient's genotype at a particular gene variance or variances, and to further ascertain whether, in the study population, particular variances are associated with particular clinical or physiological responses. The consent form should also describe procedures for assuring privacy and confidentiality of genetic information.

The US FDA reviews proposed clinical trials through the process of an Investigational New Drug Application (IND). The IND is composed of the investigator's brochure, the supporting *in vitro* and *in vivo* animal or previous human data, the clinical protocol, and the informed consent forms. In each of the sections of the IND, a specific description of a single allelic variance or a number of variances to be tested in the clinical study will be included. For example, in the investigator's brochure a description of the gene or genes hypothesized to account, at least in part, for differential responses will be included as well as a description of a genetic variance or variances in one or more candidate genes. Further, the preclinical data may include a description of *in vivo*, *in vitro* or *in silico* studies of the biochemical or physiologic effects of a variance or variances (e.g., haplotype) in a candidate gene or genes, as well as the predicted effects of the variance or variances on efficacy or toxicology of the candidate therapeutic intervention. The results of retrospective genetic analysis of response data in patients treated with the candidate therapy may be the basis for formulating the genetic hypotheses to be tested in the prospective trial. The US FDA reviews applications with particular attention to safety and toxicological data to ascertain whether candidate compounds should be tested in humans.

The established phases of clinical development are Phase I, II, III, and IV. The fundamental objectives for each phase become increasingly complex as the stages of clinical development progress. In Phase I, safety in humans is the primary focus. In these studies, dose-ranging designs establish whether the candidate therapeutic intervention is safe in the suspected therapeutic concentration range. However, it is common practice to obtain information about surrogate markers of efficacy even in phase I clinical trials. In a pharmacogenetic clinical trial there may be an analysis of the effect of a variance or variances on Phase I safety or surrogate

efficacy parameters. At the same time, evaluation of pharmacokinetic parameters (e.g., adsorption, distribution, metabolism, and excretion) may be a secondary objective; again, in a pharmacogenetic clinical study there may be an analysis of the effect of sequence variation in genes that affect absorption, distribution, metabolism and excretion of the candidate compound on pharmacokinetic parameters such as peak blood levels, half life or tissue distribution of the compound. As clinical development stages progress, trial objectives focus on the appropriate dose and method of administration required to elicit a clinically relevant therapeutic response. In a pharmacogenetic clinical trial, there may be a comparison of the effectiveness of several doses of a compound in patients with different genotypes, in order to identify interactions between genotype and optimal dose. For this purpose the doses selected for late stage clinical testing may be greater, equal or less than those chosen based upon preclinical safety and efficacy determinations. Data on the function of different alleles of genes affecting pharmacokinetic parameters could provide the basis for selecting an optimal dose or range or doses of a compound or biological. Genes involved in drug metabolism may be particularly useful to study in relation to understanding interpatient variation in optimal dose. Genes involved in drug metabolism include the cytochrome P450s, especially 2D6, 3A4, 2C9, 2E1, 2A6 and 1A1; the glucuronyltransferases; the acetyltransferases; the methyltransferases; the sulfotransferases; the glutathione system; the flavine monooxygenases and other enzymes known in the art.

An additional objective in the latter stages of clinical development is demonstration of the effect of the therapeutic intervention on a broad population. In phase III trials, the number of individuals enrolled is dictated by a power analysis. The number of patients required for a given pharmacogenetic clinical trial will be determined by prior knowledge of variance or haplotype frequency in the study population, likely response rate in the treated population, expected magnitude of pharmacogenetic effect (for example, the ratio of response rates between a genetic subgroup and the unfractionated population, or between two different genetic subgroups); nature of the genetic effect, if known (e.g. dominant effect, codominant effect, recessive effect); and number of genetic hypotheses to be evaluated (including number of genes and/or variances to be studied, number of gene or variance interactions to be studied). Other considerations will likely arise in the design of specific trials.

Clinical trials should be designed to blind both human subjects and study coordinators from biasing that may otherwise occur during the testing of a candidate therapeutic invention. Often the candidate therapeutic intervention is compared to best medical treatment, or a placebo (a compound, agent, device, or procedure that

appears identical to the candidate therapeutic intervention but is therapeutically inert). The combination of a placebo group and blind controls for potentially confounding factors such as prejudice on the part of study participants or investigators, insures that real, rather than perceived or expected, effects of the candidate therapeutic intervention are measured in the trials. Ideally blinding extends not only to trial subjects and investigators but also to data review committees, ancillary personnel, statisticians, and clinical trial monitors.

In pharmacogenetic clinical studies, a placebo arm or best medical control group may be required in order to ascertain the effect of the allelic variance or variances on the efficacy or toxicology of the candidate therapeutic intervention as well as placebo or best medical therapy. It will be important to assure that the composition of the control and test populations are matched, to the degree possible, with respect to genetic background and allele frequencies. This is particularly true if the variances being investigated may have an effect on disease manifestations (in addition to a hypothesized effect on response to treatment). It is likely that standard clinical trial procedures such as insuring that treatment and control groups are balanced for race, sex and age composition and other non-genetic factors relevant to disease will be sufficient to assure that genetic background is controlled, however a preferred practice is to explicitly test for genetic stratification between test and control groups. Methods for minimizing the possibility of spurious results attributable to genetic stratification between two comparison groups include the use of surrogate markers of geographic, racial and/or ethnic background, such as have been described by Rannala and coworkers. (See, for example: Rannala B, and JL Mountain. 1997 Detecting immigration by using multilocus genotypes. *Proc Natl Acad Sci U S A* Aug 19;94(17):9197-201.) One procedure would be to assure that surrogate markers of genetic background (such as those described by Rannala and Mountain) occur at comparable frequency in two comparison groups.

Open label trials are unblinded; in single blind trials patients are kept unaware of treatment assignments; in double blind trials both patients and investigators are unaware of the treatment groups; a combination of these procedures may be instituted during the trial period. Pharmacogenetic clinical trial design may include one or a combination of open label, single blind, or double blind clinical trial designs. Reduction of biases attributable to the knowledge of either the type of treatment or the genotype of the normal subjects or patients is an important aspect of study design. So, for example, even in a study that is single blind with respect to treatment, it should be possible to keep both patients and caregivers blinded to genotype during the study.

In designing a clinical trial it is important to include termination endpoints

such as adverse clinical events, inadequate study participation either in the form of lack of adherence to the clinical protocol or loss to follow up, (e.g. such that adequate power is no longer assured), lack of adherence on the part of trial investigators to the trial protocol, or lack of efficacy or positive response within the test group. In a pharmacogenetic clinical trial these considerations obtain not only in the entire treatment group, but also in the genetically defined subgroups. That is, if a dangerous toxic effect manifests itself predominantly or exclusively in a genetically defined subpopulation of the total treatment population it may be deemed inappropriate to continue treating that genetically defined subgroup. Such decisions are typically made by a data safety monitoring committee, a group of experts not including the investigators, and generally not blinded to the analysis, who review the data from an ongoing trial on a regular basis.

It is important to note that medicine is a conservative field, and clinicians are unlikely to change their behavior on the basis of a single clinical trial. Thus it is likely that, in most instances, two or more clinical trials will be required to convince physicians that they should change their prescribing habits in view of genetic information. Large scale trials represent one approach to providing increased data supporting the utility of a genetic stratification. In such trials the stringent clinical and laboratory data collection characteristic of traditional trials is often relaxed in exchange for a larger patient population. Important goals in large scale pharmacogenetic trials will include establishing whether a pharmacogenetic effect is detectable in all segments of a population. For example, in the North American population one might seek to demonstrate a pharmacogenetic effect in people of African, Asian, European and Hispanic (i.e. Mexican and Puerto Rican) origin, as well as in native American people. (It generally will not be practical to segment patients by geographical origin in a standard clinical trial, due to loss of power.) Another goal of a large scale clinical trial may be to measure more precisely, and with greater confidence, the magnitude of a pharmacogenetic effect first identified in a smaller trial. Yet another undertaking in a large scale clinical trial may be to examine the interaction of an established pharmacogenetic variable (e.g. a variance in gene A, shown to affect treatment response in a smaller trial) with other genetic variances (either in gene A or in other candidate genes). A large scale trial provides the statistical power necessary to test such interactions.

In designing all of the above stages of clinical testing investigators must be attentive to the statistical problems raised by testing multiple different hypotheses, including multiple genetic hypotheses, in subsets of patients. Bonferroni's correction or other suitable statistical methods for taking account of multiple hypothesis testing will need to be judiciously applied. However, in the early stages

of clinical testing, when the main goal is to reduce the large number of potential hypotheses that could be tested to a few that will be tested, based on limited data, it may be impractical to rigidly apply the multiple testing correction.

B. Phase I Clinical Trials

1. Introduction

Phase I of clinical development is generally focused on safety, although drug companies are increasingly obtaining information on pharmacokinetics and surrogate pharmacodynamic markers in early trials. Phase I studies are typically performed with a small number (< 60) of normal, healthy volunteers usually at single institutions. The primary endpoints in these studies usually relate to pharmacokinetic parameters (i.e. adsorption, distribution, metabolism and bioavailability), and dose-related side effects. In a Phase I pharmacogenetic clinical trial, stratification based upon allelic variance or variances of a candidate gene or genes related to pharmacokinetic parameters may allow early assessment of potential genetic interactions with treatment.

Phase I studies of some diseases (e.g. cancer or other medically intractable diseases for which no effective medical alternative exists) may include patients who satisfy specified inclusion criteria. These safety/limited-efficacy studies can be conducted at multiple institutions to ensure rapid enrollment of patients. In a pharmacogenetic Phase I study that includes patients, or a mixture of patients and normals, the status of a variance or variances suspected to affect the efficacy of the candidate therapeutic intervention may be used as part of the inclusion criteria. Alternatively, analysis of variances or haplotypes in patients with different treatment responses may be among the the endpoints. It is not unusual for such a Phase I study design to include a double-blind, balanced, random-order, crossover sequence (separated by washout periods), with multiple doses on separate occasions and both pharmacokinetic and pharmacodynamic endpoints.

2. Phase I trials with subjects drawn from large populations and/or from related volunteer subjects: the Pharmacogenetic Phase I Unit concept

In general it is useful to be able to assess the contribution of genetic variation to treatment response at the earliest possible stage of clinical development. Such an assessment, if accurate, will allow efficient prioritization of candidate compounds for subsequent detailed pharmacogenetic studies; only those treatments where there is early evidence of a significant interaction of genetic variation with treatment response would be advanced to pharmacogenetic studies in later stages of development. In this invention we describe methods for achieving early insight – in

Phase I - into the contribution of genetic variation to variation in surrogate treatment response variables. It occurred to the inventors that this can be accomplished by bringing the power of genetic linkage analysis and outlier analysis to Phase I testing via the recruitment of a very large Phase I population including a large number of individuals who have consented in advance to genetic studies (occasionally referred to hereinafter as a Pharmacogenetic Phase I Unit). In one embodiment of a Pharmacogenetic Phase I Unit many of the subjects are related to each other by blood. (Currently Phase I trials are performed in unrelated individuals, and there is no consideration of genetic recruitment criteria, or of genetic analysis of surrogate markers.) There are several novel ways in which a large population, or a population comprised at least in part of related individuals, could be useful in early clinical trials. Some of the most attractive applications depend on the availability of surrogate markers for pharmacodynamic drug action which can be used early in clinical development, preferably in normal subjects in Phase I. Such surrogate markers are increasingly used in Phase I, as drug development companies seek to make early yes/no decisions about compounds.

Recruitment of a population optimized for clinical genetic investigation may entail utilization of methods in statistical genetics to select the size and composition of the population. For example powerful methods for detecting and mapping quantitative trait loci in sibpairs have been developed. These methods can provide some estimate of the statistical power derived from a given number of groups of closely related individuals. Ideally subjects in the pharmacogenetic Phase I unit are of known ethnic/racial/geographic background and willing to participate in Phase I studies, for pay, over a period of years. The population is preferably selected to achieve a specified degree of statistical power for genetic association studies, or is selected in order to be able to reliably identify a certain number of individuals with rare genotypes, as discussed below. Family participation could be encouraged by appropriate incentive compensation. For example, individual subjects might be paid \$200 for participation in a study; two sibs participating in the same study might each be paid \$300; if they could encourage another sib (or cousin) to participate the three related individuals might each be paid \$350, and so forth. This type of compensation would encourage subjects to recruit their relatives to participate in Phase I studies. (It would also increase the cost of studies, however the type of data that can be obtained can not be duplicated with conventional approaches.) The optimal location to establish such a Phase I unit is a city with a stable population, many large families, and a positive attitude about gene technology. The Pharmacogenetic Phase I Unit population can then be used to test for the existence of genetic variation in response to any drug as a first step in deciding whether to

proceed with extensive pharmacogenetic studies in later stages of clinical development. Specific uses of a large Phase I unit in which some or all subjects are related include:

a. It should be possible, for virtually any compound, to assess the magnitude of the genetic contribution to variation in drug response (if any) by comparing variation in drug response traits among related vs. non-related individuals. The rationale is as follows: if a surrogate drug response trait (i.e. a surrogate marker of pharmacodynamic effect that can be measured in normal subjects) is under strong genetic control then related individuals, who share 25% (cousins) or 50% (sibs) of their alleles, should have less divergent responses (less intragroup variance) than unrelated individuals, who share a much smaller fraction of alleles. That is, individuals who share alleles at the genes that affect drug response should be more similar to each other (i.e. have a narrower distribution of responses, whether measured by variance, standard deviation or other means) than individuals who, on average, share very few alleles. By using statistical methods known in the art the degree of variation in a set of data from related individuals (each individual would only be compared with his/her relatives, but such comparisons would be performed within each group of relatives and a summary statistic developed) could be compared to the degree of variation in a set of unrelated individuals (the same subjects could be used, but the second comparison would be across related groups). Account would be taken of the degree of similarity expected between related individuals, based on the fraction of the genome they shared by descent. Thus the extent of variation in the surrogate response marker between identical twins should be less than between sibs, which should be less than between first cousins, which should be less than that between second cousins, and so forth, *if* there is a genetic component to the variation. It is well known from twin studies (in which, for example, variation between identical twins is compared to variation between fraternal twins) that pharmacokinetic variables (e.g. compound half life, peak concentration) are frequently over 90% heritable; the type of study proposed here (comparison of variation within groups of sibs and cousins to variation between unrelated subjects) would also show this genetic effect, without requiring the recruitment of monozygotic twins. For a summary of pharmacokinetic studies in twins see: Propping, Paul (1978) *Pharmacogenetics. Rev. Physiol. Biochem. Pharmacol.* 83: 123-173.

It may be that the pattern of drug responses that distinguishes related individuals from non-related individuals is more complex than, for example, variance or standard deviation. For example, there may be two discrete phenotypes characteristic of intrafamilial variation (a bimodal distribution) that are not a feature

of variation between unrelated individuals (where, for example, variation might be more nearly continuous). Such a pattern could be attributable to Mendelian inheritance operating on a restricted set of alleles in a family (or families) with, for example, AA homozygotes giving one phenotype and AB heterozygotes and BB homozygotes giving a second phenotype, all in the context of a relatively homogeneous genetic background. In contrast, variation among non-related subjects would be less discrete due to a greater degree of variation in genetic background and the presence of additional alleles C, D and E at the candidate locus. Statistical measures of the significance of such differences in distribution, including nonparametric methods such as chi square and contingency tables, are known in the art.

The methods described herein for measuring whether pharmacodynamic traits are under genetic control, using surrogate markers of drug efficacy in phase I studies which include groups of related individuals, will be useful in obtaining an early assessment of the extent of genetically determined variation in drug response for a given therapeutic compound. Such information provides an informed basis for either stopping development at the earliest possible stage or, preferably, continuing with development but with a plan for identifying and controlling for genetic variation so as to allow rapid progression through the regulatory approval process.

For example, it is well known that Alzheimers trials are long and expensive, and most drugs are only effective in a fraction of patients. Using surrogate measures of response in normals drawn from a population of related individuals would help to assess the contribution of genetic variation to variation in treatment response. For an acetylcholinesterase inhibitor, relevant surrogate pharmacodynamic measures could include testing erythrocyte membrane acetylcholinesterase levels in drug treated normal subjects, or performing psychometric tests that are affected by treatment (and ideally that correlate with clinical efficacy) and measuring the effect of treatment. As another example, antidepressant drugs can produce a variety of effects on mood in normal subjects – or no effect at all. Careful monitoring and measurement of such responses in related vs. unrelated normal subjects, and statistical comparison of the degree of variation in each group, could provide an early readout on whether there is a genetic component to drug response (and hence clinical efficacy). The observation of similar effects in family members, and comparatively dissimilar effects in unrelated subjects would provide compelling evidence of a pharmacogenetic effect and justify the substantial expenditure necessary for a full pharmacogenetic drug development program. Conversely, the absence of any significant family influence on drug response would provide an early termination point for pharmacogenetic studies. *Note that the proposed studies do*

not require any knowledge of candidate genes, nor is DNA collection or genotyping required – simply a reliable surrogate pharmacodynamic assay and small groups of related normal individuals. Refined statistical methods should permit the magnitude of the pharmacogenetic effect to be measured, which could be a further criteria for deciding whether to proceed with pharmacogenetic analysis. The greater the differential in magnitude or pattern of variance between the related and the unrelated subjects, the greater the extent of genetic control of the trait.

Not all drug response traits are under the predominant control of one locus. Many such traits are under the control of multiple genes, and may be referred to as quantitative trait loci. It is then desirable to identify the major loci contributing to variation in the drug response trait. This can be done for example, to map quantitative trait loci in a population of drug treated related normals. Either a candidate gene approach or a genome wide scanning approach can be used. (For review of some relevant methods see: Hsu L, Aragaki C, Quiaoit F. (1999) A genome-wide scan for a simulated data set using two newly developed methods. *Genet Epidemiol* 17 Suppl 1:S621-6; Zhao LP, Aragaki C, Hsu L, Quiaoit F. (1998) Mapping of complex traits by single-nucleotide polymorphisms. *Am J Hum Genet* 63(1):225-40; Stoesz MR, Cohen JC, Mooser V, et al. (1997) Extension of the Haseman-Elston method to multiple alleles and multiple loci: theory and practice for candidate genes. *Ann Hum Genet* 61 (Pt 3):263-74.)) However, this method would require at least 100 patients (preferably 200, and still more preferably >300) to have adequate statistical power, and each patient would have to be genotyped at a few polymorphic loci (candidate gene approach) or hundreds of polymorphic loci (genome scanning approach).

b. With a large Phase I population of normal subjects that need not be related (a second type of Pharmacogenetic Phase I Unit) it is possible to efficiently identify and recruit for any Phase I trial a set of individuals comprising virtually any combination of genotypes present in a population (for example, all common genotypes, or a group of genotypes expected to represent outliers for a drug response trait of interest). This method preferably entails obtaining blood or other tissue (e.g. buccal smear) in advance from a large number of the subjects in the Phase I unit. Ideally consent for genotyping would be obtained at the same time. It would be most efficient if blanket consent for genotyping any polymorphic site or sites could be obtained. Second best would be consent for testing any site relevant to any customer project (not specific at the time of initial consent). Third best would be consent to genotype polymorphic sites relevant to specific disease areas. Another, less desirable, solution would be to obtain consent for genotyping on a project by

project basis (for example by mailing out reply cards), after the specific polymorphic sites to be genotyped are known.

One useful way to screen for pharmacogenetic effects in Phase I is to recruit homozygotes for a variance or variances of interest in one or more candidate genes. For example, consider a compound for which there are two genes that are strong candidates for influencing response to treatment. Gene X has alleles A and A', while gene Y has alleles B and B'. If these genes do in fact contribute significantly to response then one would expect that, regardless of the mode of inheritance (recessive, codominant, dominant; polygenic) homozygotes would exhibit the most extreme responses. One would also expect epistatic interactions, if any, to be most extreme in double homozygotes. Thus one would ideally perform a surrogate drug response test in Phase I volunteers doubly homozygous at both X and Y. That is, test AA/BB, A'A'/BB, AA/B'B' and A'A'/B'B' subjects. If the allele frequencies for A and A' are .15 and .85, and for B and B' .2 and .8 then the frequency of AA homozygotes is expected to be 2.25% and BB homozygotes 4%. In the absence of any linkage between the genes, the frequency of AA/BB double homozygotes is expected to be $0.0225 \times 0.04 = 0.0009$ or .09%, or about 1 subject in 1000. Ideally at least 5 subjects of each genotype are recruited for the Phase I study, and preferably at least 10 subject. Thus, even for variances of moderately low allele frequency (15%, 20%), the identification of potential outliers (i.e. homozygotes) for the candidate genes of interest will require a large population. Preferably the Phase I unit has enrolled at least 1,000 normal individuals, more preferably 2,000, still more preferably 5,000 and most preferably 10,000 or more. In another application of the large, genotyped Phase I population it may be useful to identify individuals with rare variances in candidates genes (either homozygous or heterozygous), in order to determine whether those variances are predisposing to extreme pharmacological responses to the compound. For example, variances occurring at 5% allele frequency are expected to occur in homozygous form in 0.25% of the population (0.05×0.05), and therefore may rarely, if ever, be encountered in early clinical development. Yet it may be serious adverse effects occurring in just such a small group that create problems in later stages of drug development. In yet another application of the large genotyped Phase I population, subjects may be selected to represent the known common variances in one or more genes that are candidates for influencing the response to treatment. By insuring that all common genotypes are represented in a Phase I trial the likelihood of misleading results due to genetic stratification (resulting in discrepancy with results of later, larger trials can be reduced.

It would be useful to prospectively genotype the large Phase I population for variances that are commonly the source of interpatient variation in drug response, since demand for genotyped groups of such patients can be anticipated from pharmaceutical companies and contract research organizations (CROs). For example, genotyping might initially focus on common pharmacological targets such as estrogen receptors, adrenergic receptors, or serotonin receptors. The pre-genotyped Phase I population could be part of a package of services (along with genotyping assay development capability, high throughput genotyping capacity and software and expertise in statistical genetics) designed to accelerate pharmacogenetic Phase I studies. Eventually, as the databank of genotypes built up, individuals with virtually any genotype or combination of genotypes could be called in for precisely designed physiological or toxicological studies designed to test for pharmacogenetic effects.

One of the most useful aspects of the Pharmacogenetic Phase I Unit is that subjects with rare genotypes can be pharmacologically assessed in a small study. This addresses a serious limitation of conventional clinical trials with respect to the investigation of polygenic traits or the effect of rare alleles. Unfortunately even Phase III studies, as currently performed, are often barely powered to address simple one variance hypotheses about efficacy or toxicity. The problem, of course, is that each time a new genetic variable is introduced the comparison groups are cut in halves or thirds (or even smaller groups if there are multiple haplotypes at each gene). It is therefore a challenging problem to test the interaction of several genes in determining drug response. Yet the character of drug response data in populations -- there is often a continuous distribution of responses among different individuals -- suggests that drug responses may often be mediated by several genes. (On the other hand, there are an increasing number of well documented single gene, or even single variance, pharmacogenetic effects in the literature, showing that it is possible to detect the effect of a single variance.) One approach to identifying pharmacogenetic effects is to focus on finding the single gene variances that have the largest effects. This approach can be undertaken within the scale of current clinical trials. However, in order to develop a test which predicts a large fraction of the quantitative variation in a drug response trait it may be desirable to test the effect of multiple genes, including the interaction of variances at different genes, which may be non-additive (referred to as epistasis). The Pharmacogenetic Phase I Unit provides a way to efficiently test for gene interactions or multigene effects by, for example, allowing easy identification of individuals who, on account of being homozygous at several loci of interest, should be outliers for the drug response phenotypes of interest if there is a gene x gene interaction. Testing drug response in a small number of such

individuals will provide a quick read on gene interaction. Obtaining genetic data on the pharmacodynamic action of a compound in Phase I should also provide a crude measure of allele effects – which variances or haplotypes increase pharmacological responses and which decrease them. This information is of great value in designing subsequent trials, as it constrains the number of hypotheses to be tested, thereby enabling powerful statistical designs. This is because when the effect of variances on drug response measures is unknown one is forced to statistically test all the possible effects of each allele (e.g. two tailed tests). As the number of genetically defined groups increases (e.g. as a result of multiple variances or haplotypes) there is a loss of statistical power due to multiple testing correction. On the other hand, if the relative phenotypic effect of each allele at a locus is known (or can be hypothesized) from Phase I data then each individual in a subsequent clinical trial contributes useful information – there is a specific prediction of response based on that individuals combination of genotypes or haplotypes, and testing the fit of the actual data to those predictions provides for powerful statistical designs. (It is also possible to measure allele effects biochemically, of course, to establish which alleles have positive and which negative effects, but at considerable cost.)

It is important to note that Phase I trials can provide useful information at almost any stage of clinical development. It is not unusual, for example, for a product in Phase II or even Phase III testing to be remanded to Phase I in order to clarify some aspect of toxicology or physiology. In this context a Pharmacogenetic Phase I Unit would be extremely useful to a drug development company. Phase I studies in defined genetic subgroups drawn from a large genotyped population, or in groups of related individuals, would be the most economical and efficient way to clarify the existence of pharmacogenetic effects, if any, paving the way for future rational development of the product.

C. Phase II Clinical Trials

Phase II studies generally include a limited number of patients (<100) who satisfy a set of predefined inclusion criteria and do not satisfy any predefined exclusion criteria of the trial protocol. Phase II studies can be conducted at single or multiple institutions. Inclusion/exclusion criteria may include historical, clinical and laboratory parameters for a disease, disorder, or condition; age; gender; reproductive status (i.e. pre- or postmenopausal); coexisting medical conditions; psychological, emotional or cognitive state, or other objective measures known to those skilled in the art. In a pharmacogenetic Phase II trial the inclusion/exclusion criteria may include one or more genotypes or haplotypes. Alternatively, genetic analysis may

be performed at the end of the trial. The primary goals in Phase II testing may include (i) identification of the optimal medical indication for the compound, (ii) definition of an optimal dose or range or doses, balancing safety and efficacy considerations (dose-finding studies), (iii) extended safety studies (complementing Phase I safety studies), (iv) evaluation of efficacy in patients with the targeted disease or condition, either in comparison to placebo or to current best therapy. To some extent these goals may be achieved by performing multiple trials with different goals. Likewise, Phase II trials may be designed specifically to evaluate pharmacogenetic aspects of the drug candidate. Primary efficacy endpoints typically focus on clinical benefit, while surrogate endpoints may measure treatment response variables such as clinical or laboratory parameters that track the progress or extent of disease, often at lesser time, cost or difficulty than the definitive endpoints. A good surrogate marker must be convincingly associated with the definitive outcome. Examples of surrogate endpoints include tumor size as a surrogate for survival in cancer trials, and cholesterol levels as a surrogate for heart disease (e.g. myocardial infarction) in trials of lipid lowering cardiovascular drugs. Secondary endpoints supplement the primary endpoint and may be selected to help guide further clinical studies.

In a pharmacogenetic Phase II clinical trial, retrospective or prospective design will include the stratification of patients based upon a variance or variances in a gene or genes suspected of affecting treatment response. The gene or genes may be involved in mediating pharmacodynamic or pharmacokinetic response to the candidate therapeutic intervention. The parameters evaluated in the genetically stratified trial population may include primary, secondary or surrogate endpoints. Pharmacokinetic parameters - for example, dosage, absorption, toxicity, metabolism, or excretion - may also be evaluated in genetically stratified groups.. Other parameters that may be assessed in parallel with genetic stratification include gender, race, ethnic or geographic origin (population history) or other demographic factors.

While it is optimal to initiate pharmacogenetic studies in phase I, as described above, it may be the case that pharmacogenetic studies are not considered until phase II, when problems relating either to efficacy or toxicity are first encountered. It is highly desirable to initiate pharmacogenetic studies no later than Phase II of a clinical development plan because (1) phase III studies tend to be large and expensive - not an optimal setting in which to explore untested pharmacogenetic hypotheses; (2) phase III studies are typically designed to test one fairly narrow hypothesis regarding efficacy of one or a few dose levels in a specific disease or condition. Phase II studies are often numerous, and are intended to

provide a broad picture of the pharmacology of the candidate compound. This is a good setting for initial pharmacogenetic studies. Several pharmacogenetic hypotheses may be tested in phase II, with the goal of eliminating all but one or two.

5 D. Phase III Clinical Trials

Phase III studies are generally designed to measure efficacy of a new treatment in comparison to placebo or to an established treatment method. Phase II studies are often performed at multiple sites. The design of this type of trial includes power analysis to ensure the sufficient data will be gathered to demonstrate the anticipated effect, making assumptions about response rate based on earlier trials. As a result Phase III trials frequently include large numbers of patients (up to 5,000). Primary endpoints in Phase III studies may include reduction or arrest of disease progression, improvement of symptoms, increased longevity or increased disease-free longevity, or other clinical measures known in the art. In a pharmacogenetic Phase III clinical study, the endpoints may include determination of efficacy or toxicity in genetically defined subgroups. Preferably the genetic analysis of outcomes will be confined to an assessment of the impact of a small number of variances or haplotypes at a small number of genes, said variances having already been statistically associated with outcomes in earlier trials. Most preferably variances at only one or two genes will be assessed.

After successful completion of one or more Phase III studies, the data and information from all trials conducted to test a new treatment method are compiled into a New Drug Application (NDA) and submitted for review by the US FDA, which has authority to grant marketing approval in the US and its territories. The NDA includes the raw (unanalyzed) clinical data, i.e. the patient by patient measurements of primary and secondary endpoints, a statistical analysis of all of the included data, a document describing in detail any observed side effects, tabulation of all patients who dropped-out of trials and detailed reasons for their termination, and any other available data pertaining to ongoing *in vitro* or *in vivo* studies since the submission of the investigational new drug (IND) application. If pharmacoeconomic objectives are a part of the clinical trial design then data supporting cost or economic analyses are included in the NDA. In a pharmacogenetic clinical study, the pharmacoeconomic analyses may include genetically stratified assessment of the candidate therapeutic intervention in a cost benefit analysis, cost of illness study, cost minimization study, or cost utility analysis. The analysis may also be simultaneously stratified by standard criteria such as race/ethnicity/geographic origin, sex, age or other criteria. Data from a genetically stratified analysis may be used to support an application for approval for

marketing of the candidate therapeutic intervention.

E. Phase IV Clinical Trials

Phase IV studies occur after a therapeutic intervention has been approved for marketing, and are typically conducted for surveillance of safety, particularly occurrence of rare side effects. The other principal reason for Phase IV studies is to produce information and relationships useful for marketing a drug. In this regard pharmacogenetic analysis may be very useful in Phase IV trials. Consider, for example, a drug that is the fourth or fifth member of a drug class (say statins, or thiazidinediones or fluoropyrimidines) to obtain marketing approval, and which does not differ significantly in clinical effects – efficacy or safety - from other members of the drug class. The first, second and third drugs in the class will likely have a dominant market position (based on their earlier introduction into the marketplace) that is difficult to overcome, particularly in the absence of differentiating clinical effects. However, it is possible that the new drug produces a superior clinical effect – for example, higher response rate, greater magnitude of response or fewer side effects - in a genetically defined subgroup. The genetic subgroup with superior response may constitute a larger fraction of the total patient population than the new drug would likely achieve otherwise. In this instance, there is a clear rationale for performing a Phase IV pharmacogenetic trial to identify a variance or variances that mark a patient population with superior clinical response. Subsequently a marketing campaign can be designed to alert patients, physicians, pharmacy managers, managed care organizations and other parties that, with the use of a rapid and inexpensive genetic test to identify eligible patients, the new drug is superior to other members of the class (including the market leading first, second and third drugs introduced). The high responder subgroup defined by a variance or variances may also exhibit a superior response to other drugs in the class (a class pharmacogenetic effect), or the superior efficacy in the genetic subgroup may be specific to the drug tested (a compound-specific pharmacogenetic effect).

In a Phase IV pharmacogenetic clinical trial, both retrospective and prospective analysis can be performed. In both cases, the key element is genetic stratification based on a variance or variances or haplotype. Phase IV trials will often have adequate sample size to test more than one pharmacogenetic hypothesis in a statistically sound way.

F. Unconventional Clinical Development

Although the above listed phases of clinical development are well-established, there are cases where strict Phase I, II, III development does not occur,

for example, in the clinical development of candidate therapeutic interventions for debilitating or life threatening diseases, or for diseases where there is presently no available treatment. Some of the mechanisms established by the FDA for such studies include Treatment INDs, Fast-Track or Accelerated reviews, and Orphan Drug Status. In a clinical development program for a candidate therapeutic of this type there is a useful role for pharmacogenetic analysis, in that the candidate therapeutic may not produce a sufficient benefit in all patients to justify FDA approval, however analysis of outcome in genetic subgroups may lead to identification of a variance or variances that predict a response rate sufficient for FDA approval.

As used herein, "supplemental applications" are those in which a candidate therapeutic intervention is tested in a human clinical trial in order to gain an expanded label indication, expanding recommended use to new medical indications. In these applications, previous clinical studies of the therapeutic intervention, i.e. preclinical safety and Phase I human safety studies can be used to support the testing of the therapeutic intervention in a new indication. Pharmacogenetic analysis is also useful in the context of clinical trials to support supplemental applications. Since these are, by definition, focused on diseases not selected for initial development the overall efficacy may not be as great as for the leading indication(s). The identification of genetic subgroups with high response rates may enable the rapid approval of supplemental applications for expanded label indications. In such instances part of the label indication may be a description of the variance or variances that define the group with superior response.

As used herein, "outcomes" or "therapeutic outcomes" describe the results and value of healthcare intervention. Outcomes can be multi-dimensional, and may include improvement of symptoms; regression of a disease, disorder, or condition; prevention of a disease or symptom; cost savings or other measures.

Pharmacoeconomics is the analysis of a therapeutic intervention in a population of patients diagnosed with a disease, disorder, or condition that includes at least one of the following studies: cost of illness study (COI); cost benefit analysis (CBA), cost minimization analysis (CMA), or cost utility analysis (CUA), or an analysis comparing the relative costs of a therapeutic intervention with one or a group of other therapeutic interventions. In each of these studies, the cost of the treatment of a disease, disorder, or condition is compared among treatment groups. Costs have both direct (therapeutic interventions, hospitalization) and indirect (loss of productivity) components. Pharmacoeconomic factors may provide the motivation for pharmacogenetic analysis, particularly for expensive therapies that benefit only a fraction of patients. For example, interferon alpha is the only

treatment that can cure hepatitis C virus infection, however viral infection is completely and permanently eliminated in less than a quarter of patients. Nearly half of patients receive virtually no benefit from alfa interferon, but may suffer significant side effects. Treatment costs are ~\$10,000 per course. A
5 pharmacogenetic test that could predict responders would save much of the cost of treating patients not able to benefit from interferon alpha therapy, and could provide the rationale for treating a population in a cost efficient manner, where treatment would otherwise be unaffordable.

As used herein, "health-related quality of life" is a measure of the impact of a
10 disease, disorder, or condition on a patient's activities of daily living. An analysis of the health-related quality of life is often included in pharmacoeconomic studies.

As used herein, the term "stratification" refers to the partitioning of patients into groups on the basis of clinical or laboratory characteristics of the patient.
"Genetic stratification" refers to the partitioning of patients or normal subjects into
15 groups based on the presence or absence of a variance or variances in one or more genes. The stratification may be performed at the end of the trial, as part of the data analysis, or may come at the beginning of a trial, resulting in creation of distinct groups for statistical or other purposes.

20 *G. Power analysis in pharmacogenetic clinical trials*

The basic goal of power calculations in clinical trial design is to insure that trials have adequate patients and controls to fairly assess, with statistical significance, whether the candidate therapeutic intervention produces a clinically significant benefit.

25 Power calculations in clinical trials are related to the degree of variability of the drug response phenotypes measured and the treatment difference expected between comparison groups (e.g. between a treatment group and a control group). The smaller the variance within each group being compared, and the greater the difference in response between the two groups, the fewer patients are required to
30 produce convincing evidence of an effect of treatment. These two factors (variance and treatment difference) determine the degree of precision required to answer a specific clinical question.

The degree of precision may be expressed in terms of the maximal acceptable standard error of a measurement, the magnitude of variation in which the
35 95% confidence interval must be confined or the minimal magnitude of difference in a clinical or laboratory value that must be detectable (at a statistically significant level, and with a specified power for detection) in a comparison to be performed at

the end of the trial (hypothesis test). The minimal magnitude is generally set at the level that represents the minimal difference that would be considered of clinical importance.

In pharmacogenetic clinical trials there are two countervailing effects with respect to power. First, the comparison groups are reduced in size (compared to a conventional trial) due to genetic partitioning of both the treatment and control groups into two or more subgroups. However, it is reasonable to expect that variability for a trait is smaller within groups that are genetically homogeneous with respect to gene variances affecting the trait. If this is the case then power is increased as a function of the reduction in variability within (genetically defined) groups.

In general it is preferable to power a pharmacogenetic clinical trial to see an effect in the largest genetically defined subgroups. For example, for a variance with allele frequencies of 0.7 and 0.3 the common homozygote group will comprise 49% of all patients ($0.7 \times 0.7 \times 100$). It is most desirable to power the trial to observe an effect (either positive or a negative) in this group. If it is desirable to measure an effect of therapy in a small genetic group (for example, the 9% of patients homozygous for the rare allele) then genotyping should be considered as an enrollment criterion to insure a sufficient number of patients are enrolled to perform an adequately powered study.

Statistical methods for powering clinical trials are known in the art. See, for example: Shuster, J.J. (1990) Handbook of Sample Size Guidelines for Clinical Trials. CRC Press, Boca Raton, FL; Machin, D. and M.J. Campbell (1987) Statistical Tables for the Design of Clinical Trials. Blackwell, Oxford, UK; Donner, A. (1984) Approaches to Sample Size Estimation in the Design of Clinical Trials – A Review. *Statistics in Medicine* 3: 199-214.

H. Statistical analysis of clinical trial data

There are a variety of statistical methods for measuring the difference between two or more groups in a clinical trial. One skilled in the art will recognize that different methods are suited to different data sets. In general, there is a family of methods customarily used in clinical trials, and another family of methods customarily used in genetic epidemiological studies. Methods in quantitative and population genetics designed to measure the association between genotypes and phenotypes, and to map and measure the effect of quantitative trait loci are also relevant to the task of measuring the impact of a variance on response to a treatment. Methods from any of these disciplines may be suitable for performing statistical analysis of pharmacogenetic clinical trial data, as is known to those skilled in the art.

Conventional clinical trial statistics include hypothesis testing and descriptive methods, as elaborated below. Guidance in the selection of appropriate statistical tests for a particular data set is provided in texts such as: Biostatistics: A Foundation for Analysis in the Health Sciences, 7th edition (Wiley Series in Probability and Mathematical Statistics, Applied Probability and statistics) by Wayne W. Daniel, John Wiley & Sons, 1998; Bayesian Methods and Ethics in a Clinical Trial Design (Wiley Series in Probability and Mathematical Statistics, Applied Probability Section) by J. B. Kadane (Editor), John Wiley & Sons, 1996. Examples of specific hypothesis testing and descriptive statistical procedures that may be useful in analyzing clinical trial data are listed below.

A. Hypothesis testing statistical procedures

(1) One-sample procedures (binomial confidence interval, Wilcoxon signed rank test, permutation test with general scores, generation of exact permutational distributions)

(2) Two-sample procedures (*t*-test, Wilcoxon-Mann-Whitney test, Normal score test, Median test, Van der Waerden test, Savage test, Logrank test for censored survival data, Wilcoxon-Gehan test for censored survival data, Cochran-Armitage trend test, permutation test with general scores, generation of exact permutational distributions)

(3) R x C contingency tables (Fisher's exact test, Pearson's chi-squared test, Likelihood ratio test, Kruskal-Wallis test, Jonckheere-Terpstra test, Linear-by-linear association test, McNemar's test, marginal homogeneity test for matched pairs)

(4) Stratified 2 x 2 contingency tables (test of homogeneity for odds ratio, test of unity for the common odds ratio, confidence interval for the common odds ratio)

(5) Stratified 2 x C contingency tables (all two-sample procedures listed above with stratification, confidence intervals for the odds ratios and trend, generation of exact permutational distributions)

(6) General linear models (simple regression, multiple regression, analysis of variance -ANOVA-, analysis of covariance, response-surface models, weighted regression, polynomial regression, partial correlation, multiple analysis of variance -MANOVA-, repeated measures analysis of variance).

(7) Analysis of variance and covariance with a nested (hierarchical) structure.

(8) Designs and randomized plans for nested and crossed experiments (completely randomized design for two treatment, split-plot design, hierarchical design, incomplete block design, latin square design)

(9) Nonlinear regression models

(10) Logistic regression for unstratified or stratified data, for binary or ordinal response data, using the logit link function, the normit function or the complementary log-log function.

(11) Probit, logit, ordinal logistic and gompit regression models.

(12) Fitting parametric models to failure time data that may be right-, left-, or interval-censored. Tested distributions can include extreme value, normal and logistic distributions, and, by using a log transformation, exponential, Weibull, lognormal, loglogistic and gamma distributions.

(13) Compute non-parametric estimates of survival distribution with right-censored data and compute rank tests for association of the response variable with other variables.

B. Descriptive statistical methods

- Factor analysis with rotations
- Canonical correlation
- Principal component analysis for quantitative variables.
- Principal component analysis for qualitative data.
- Hierarchical and dynamic clustering methods to create tree structure, dendrogram or phenogram.
- Simple and multiple correspondence analysis using a contingency table as input or raw categorical data.

Specific instructions and computer programs for performing the above calculations can be obtained from companies such as: SAS/STAT Software, SAS Institute Inc., Cary, NC, USA; BMDP Statistical Software, BMDP Statistical Software Inc., Los Angeles, CA, USA; SYSTAT software, SPSS Inc., Chicago, IL, USA; StatXact & LogXact, CYTEL Software Corporation, Cambridge, MA, USA.

C. Statistical Genetic Methods Useful for Analysis of Pharmacogenetic Data

A wide spectrum of mathematical and statistical tools may be useful in the analysis of data produced in pharmacogenetic clinical trials, including methods employed in molecular, population, and quantitative genetics, as well as genetic epidemiology. Methods developed for plant and animal breeding may be useful as well, particularly methods relating to the genetic analysis of quantitative traits.

Analytical methods useful in the analysis of genetic variation among individuals, populations and species of various organisms are described in the following texts: Molecular Evolution, by W- H. Li, Sinauer Associates, Inc., 1997; Principles of Population Genetics, by D. L. Hartl and A. G. Clark, 1996; Genetics and Analysis of Quantitative Traits, By M. Lynch and B. Walsh, Sinauer Associates, Inc., Principles of Quantitative Genetics, by D. S. Falconer and T.F.C. Mackay, Longman, 1996; Genetic Variation and Human Disease, by K. M. Weiss, Cambridge University Press, 1993; Fundamentals of Genetic Epidemiology, by M. J. Khoury, T. H. Beaty, and B. H. Cohen, Oxford University Press, 1993; Handbook of Genetic Linkage, by J. Terwilliger J. Ott, Johns Hopkins University Press, 1994.

The types of statistical analysis performed in different branches of genetics are outlined below as a guide to the relevant literature and publicly available software, some of which is cited.

Molecular evolutionary genetics

- Patterns of nucleotide variation among individuals, families/populations and across species and genera,
- Alignment of sequences and description of variation/polymorphisms among the aligned sequences, amounts of similarities and dissimilarities,
- Measurement of molecular variation among various regions of a gene, testing of neutrality models,
- Rates of nucleotide changes among coding and the non-coding regions within and among populations,
- Construction of phylogenetic trees using methods such as neighborhood joining and maximum parsimony; estimation of ages of variances using coalescent models,

Population genetics

- Patterns of distribution of genes among genotypes and populations. Hardy-Weinberg equilibrium, departures from the equilibrium
- Genotype and haplotype frequencies, levels of heterozygosities, polymorphism information contents of genes, estimation of haplotypes from genotypes; the E-M algorithm, and parsimony methods
- Estimation of linkage disequilibrium and recombination
- Hierarchical structure of populations, the F-statistics, estimation of inbreeding, selection and drift
- Genetic admixture/migration and mutation frequencies
- Spatial distribution of genotypes using spatial autocorrelation methods
- Kin-structured maintenance of variation and migration

Quantitative genetics

- Phenotype as the product of the interaction between genotype and environment
- Additive, dominance and epistatic variance on the phenotype
- Effects of homozygosity, heterozygosity and developmental homeostasis
- Estimation of heritability: broad sense and narrow sense

- Determination of number of genes governing a character
- Determination of quantitative trait loci (QTLs) using family information or population information, and using linkage and/or association studies
- Determination of quantitative trait nucleotide (QTN) using a combination
linkage disequilibrium methods and cladistic approaches
- Determination of individual causal nucleotide in the diploid or haploid state on the phenotype using the method of measured genotype approaches, and combined effects or synergistic interaction of the causal mutations on the phenotype
- Determination of relative importance of each of the mutations on a given phenotype using multivariate methods, such as discriminant function, principal component and step-wise regression methods
- Determination of direct and indirect effect of polymorphisms on a complex phenotype using path analysis (partial regression) methods
- Determination of the effects of specific environment on a given genotype – genotype x environment interactions using joint regression and additive and multiplicative parameter methods.

Genetic epidemiology

- Determination of sample size based on the disease and the marker frequency in the “case” and in the “control” populations
- Stratification of study population based on gender, ethnic, socio-economic variation
- Establishing a “causal relationship” between genotype and disease, using , using various association and linkage approaches – viz., case-control designs, family studies (if available), transmission disequilibrium tests etc.,
- Linkage analysis between markers and a candidate locus using two-point and multipoint approaches.

Computer programs used for genetic analysis are: Dna SP version 3.0, by Juilo Rozas, University of Barcelona, Spain. <http://www.bio.ub.es/~Julio>; Arlequin 1.1 by S. Schnieder, J-M Kueffer, D. Roessli and L. Excoffier. University of Geneva, Switzerland, <http://anthropologie.unige.ch/arlequin>. PAUP*4, by D. L. Swofford, Sinauer Associates, Inc., 1999. SYSTAT software, SPSS Inc., Chicago, Il., 1998; . Linkage User’s Guide, by J. Ott, Rockefeller University, <http://Linkage.rockefeller.edu/soft/linkage>

Guidance in the selection of appropriate genetic statistical tests for analysis of data can be obtained from texts such as: Fundamentals of Genetic Epidemiology (Monographs in Epidemiology and Biostatistics, Vol 22) by M. J. Khoury, B. H. Cohen & T. H. Beaty, Oxford Univ Press, 1993; Methods in Genetic Epidemiology by Newton E. Morton, S. Karger Publishing, 1983; Methods in Observational Epidemiology, 2nd edition (Monographs in Epidemiology and Biostatistics, V. 26) by J. L. Kelsey (Editor), A. S. Whittemore & A. S. Evans, 1996; Clinical Trials : Design, Conduct, and Analysis (Monographs in Epidemiology and Biostatistics, Vol 8) by C. L. Meinert & S. Tonascia, 1986)

I. Retrospective clinical trials.

In general the goal of retrospective clinical trials is to test and refine hypotheses regarding genetic factors that are associated with drug responses. The best supported hypotheses can subsequently be tested in prospective clinical trials, and data from the prospective trials will likely comprise the main basis for an application to register the drug and predictive genetic test with the appropriate regulatory body. In some cases, however, it may become acceptable to use data from retrospective trials to support regulatory filings. Exemplary strategies and criteria for stratifying patients in a retrospective clinical trial are provided below.

Clinical trials to study the effect of one gene locus on drug response

A. Stratify patients by genotype at one candidate variance in the candidate gene locus.

1. Genetic stratification of patients can be accomplished in several ways, including the following (where 'A' is the more frequent form of the variance being assessed and 'a' is the less frequent form):

(a) AA vs. aa

(b) AA vs. Aa vs. aa

(c) AA vs. (Aa + aa)

(d) (AA + Aa) vs. aa.

2. The effect of genotype on drug response phenotype may be affected by a variety of nongenetic factors. Therefore it may be beneficial to measure the effect of genetic stratification in a subgroup of the overall clinical trial population.

Subgroups can be defined in a number of ways including, for example, biological, clinical, pathological or environmental criteria. For example, the predictive value of genetic stratification can be assessed in a subgroup or subgroups defined by:

a. Biological criteria:

i. gender (males vs. females)

ii. age (for example above 60 years of age). Two, three or more age groups may be useful for defining subgroups for the genetic analysis.

iii. hormonal status and reproductive history, including pre- vs. post-menopausal status of women, or multiparous vs. nulliparous women

iv. ethnic, racial or geographic origin, or surrogate markers of ethnic, racial or geographic origin. (For a description of genetic markers that serve as surrogates of racial/thnic origin see, for example: Rannala, B. and J.L. Mountain, Detecting immigration by using multilocus genotypes. *Proc Natl Acad Sci U S A*, 94 (17):

9197-9201, 1997. Other surrogate markers could be used, including biochemical markers.)

b. Clinical criteria:

i. Disease status. There are clinical grading scales for many diseases. For example, the status of Alzheimer's Disease patients is often measured by cognitive assessment scales such as the mini-mental status exam (MMSE) or the Alzheimer's Disease Assessment Scale (ADAS), which includes a cognitive component (ADAS-COG). There are also clinical assessment scales for many other diseases, including cancer.

ii. Disease manifestations (clinical presentation).

iii. Radiological staging criteria.

c. Pathological criteria:

i. Histopathologic features of disease tissue, or pathological diagnosis. (For example there are many varieties of lung cancer: squamous cell carcinoma, adenocarcinoma, small cell carcinoma, bronchoalveolar carcinoma, etc., each of which may – which, in combination with genetic variation, may correlate with

ii. Pathological stage. A variety of diseases, particularly cancer, have pathological staging schemes

iii. Loss of heterozygosity (LOH)

iv. Pathology studies such as measuring levels of a marker protein

v. Laboratory studies such as hormone levels, protein levels, small molecule levels

3. Measure frequency of responders in each genetic subgroup. Subgroups may be defined in several ways.

i. more than two age groups

ii. reproductive status such as pre or post-menopausal

4. Stratify by haplotype at one candidate locus where the haplotype is made up of two variances, three variances or greater than three variances.

Data from already completed clinical trials can be retrospectively reanalyzed. Since the questions are new, the data can be treated as if it were a prospective trial, with identified variances or haplotypes as stratification criteria or endpoints in clinically stratified data (e.g. what is the frequency of a particular variance in a response group compared to nonresponders). Care should be taken to in studying a population in which there may be a link between drug-related genes and disease-related genes.

Retrospective pharmacogenetic trials can be conducted at each of the phases

of clinical development, if sufficient data is available to correlate the physiologic effect of the candidate therapeutic intervention and the allelic variance or variances within the treatment population. In the case of a retrospective trial, the data collected from the trial can be re-analyzed by imposing the additional stratification on groups of patients by specific allelic variances that may exist in the treatment groups. Retrospective trials can be useful to ascertain whether a hypothesis that a specific variance has a significant effect on the efficacy or toxicity profile for a candidate therapeutic intervention.

A prospective clinical trial has the advantage that the trial can be designed to ensure the trial objectives can be met with statistical certainty. In these cases, power analysis, which includes the parameters of allelic variance frequency, number of treatment groups, and ability to detect positive outcomes can ensure that the trial objectives are met.

In designing a pharmacogenetic trial, retrospective analysis of Phase II or Phase III clinical data can indicate trial variables for which further analysis is beneficial. For example, surrogate endpoints, pharmacokinetic parameters, dosage, efficacy endpoints, ethnic and gender differences, and toxicological parameters may result in data that would require further analysis and re-examination through the design of an additional trial. In these cases, analysis involving statistics, genetics, clinical outcomes, and economic parameters may be considered prior to proceeding to the stage of designing any additional trials. Factors involved in the consideration of statistical significance may include Bonferroni analysis, permutation testing, with multiple testing correction resulting in a difference among the treatment groups that has occurred as a result of a chance of no greater than 20%, i.e. $p < 0.20$. Factors included in determining clinical outcomes to be relevant for additional testing may include, for example, consideration of the target indication, the trial endpoints, progression of the disease, disorder, or condition during the trial study period, biochemical or pathophysiologic relevance of the candidate therapeutic intervention, and other variables that were not included or anticipated in the initial study design or clinical protocol. Factors to be included in the economic significance in determining additional testing parameters include sample size, accrual rate, number of clinical sites or institutions required, additional or other available medical or therapeutic interventions approved for human use, and additional or other available medical or therapeutic interventions concurrently or anticipated to enter human clinical testing. Further, there may be patients within the treatment categories that present data that fall outside of the average or mean values, or there may be an indication of multiple allelic loci that are involved in the responses to the candidate therapeutic intervention. In these cases, one could propose a prospective clinical trial having an

objective to determine the significance of the variable or parameter and its effect on the outcome of the parent Phase II trial. In the case of a pharmacogenetic difference, i.e. a single or multiple allelic difference, a population could be selected based upon the distribution of genotypes. The candidate therapeutic intervention could then be tested in this group of volunteers to test for efficacy or toxicity. The repeat prospective study could be a Phase I limited study in which the subjects would be healthy human volunteers, or a Phase II limited efficacy study in which patients which satisfy the inclusion criteria could be enrolled. In either case, the second, confirmatory trial could then be used to systematically ensure an adequate number of patients with appropriate phenotype is enrolled in a Phase III trial.

A placebo controlled pharmacogenetics clinical trial design will be one in which target allelic variance or variances will be identified and a diagnostic test will be performed to stratify the patients based upon presence, absence, or combination thereof of these variances. In the Phase II or Phase III stage of clinical development, determination of a specific sample size of a prospective trial will be described to include factors such as expected differences between a placebo and treatment on the primary or secondary endpoints and a consideration of the allelic frequencies.

The design of a pharmacogenetics clinical trial will include a description of the allelic variance impact on the observed efficacy between the treatment groups. Using this type of design, the type of genetic and phenotypic relationship display of the efficacy response to a candidate therapeutic intervention will be analyzed. For example, a genotypically dominant allelic variance or variances will be those in which both heterozygotes and homozygotes will demonstrate a specific phenotypic efficacy response different from the homozygous recessive genotypic group. A pharmacogenetic approach is useful for clinicians and public health professionals to include or eliminate small groups of responders or non-responders from treatment in order to avoid unjustified side-effects. Further, adjustment of dosages when clear clinical difference between heterozygous and homozygous individuals may be beneficial for therapy with the candidate therapeutic intervention

In another example, a recessive allelic variance or variances will be those in which only the homozygote recessive for that or those variances will demonstrate a specific phenotypic efficacy response different from the heterozygotes or homozygous dominants. An extension of these examples may include allelic variance or variances organized by haplotypes from additional gene or genes.

V. Variance Identification and Use

A. Initial Identification of variances in genes

Selection of population size and composition

Prior to testing to identify the presence of sequence variances in a particular gene or genes, it is useful to understand how many individuals should be screened to provide confidence that most or nearly all pharmacogenetically relevant variances will be found. The answer depends on the frequencies of the phenotypes of interest and what assumptions we make about heterogeneity and magnitude of genetic effects. Prior to testing to identify the presence of sequence variances in a particular gene or genes, it is useful to understand how many individuals should be screened to provide confidence that most or nearly all pharmacogenetically relevant variances will be found. The answer depends on the frequencies of the phenotypes of interest and what assumptions we make about heterogeneity and magnitude of genetic effects. At the beginning we only know phenotype frequencies (e.g. responders vs. nonresponders, frequency of various side effects, etc.).

The most conservative assumption (resulting in the lowest estimate of allele frequency, and consequently the largest suggested screening population) is (i) that the phenotype (e.g. toxicity or efficacy) is multifactorial (i.e. can be caused by two or more variances or combinations of variances), (ii) that the variance of interest has a high degree of penetrance (i.e. is consistently associated with the phenotype), and (iii) that the mode of transmission is Mendelian dominant. Consider a pharmacogenetic study designed to identify predictors of efficacy for a compound that produces a 15% response rate in a nonstratified population. If half the response is substantially attributable to a given variance, and the variance is consistently associated with a positive response (in 80% of cases) and the variance need only be present in one copy to produce a positive result then ~10% of the subjects are likely heterozygotes for the variance that produces the response. The Hardy-Weinberg equation can be used to infer an allele frequency in the range of 5% from these assumptions (given allele frequencies of 5%/95% then: $2 \times .05 \times .95 = .095$, or 9.5% heterozygotes are expected, and $0.05 \times 0.05 = 0.0025$, or 0.25% homozygotes are expected. They sum to $9.5\% + 0.25\% = 9.75\%$ likely responders, 80% of whom, or 7.6%, are likely real responders due to presence of the positive response allele. Thus about half of the 15% responders are accounted for.). From the Table it can be seen that, in order to have a 99% chance of detecting an allele present at a frequency of 5% nearly 50 subjects should be screened for variances, assuming that the variances occur in the screening population at the same frequency as they occur in the patient population. Similar analyses can be performed for other assumptions regarding likely magnitude of effect, penetrance and mode of genetic transmission.

At the beginning we only know phenotype frequencies (e.g. responders vs. nonresponders, frequency of various side effects, etc.). As an example, the occurrence of serious 5-FU/FA toxicity - e.g. toxicity requiring hospitalization is often >10%. The occurrence of life threatening toxicity is in the 1-3% range (Buroker et al. 1994). The occurrence of complete remissions is on the order of 2-8%. The lowest frequency phenotypes are thus on the order of ~2%. If we assume that (i) homogeneous genetic effects are responsible for half the phenotypes of interest and (ii) for the most part the extreme phenotypes represent recessive genotypes, then we need to detect alleles that will be present at ~10% frequency ($.1 \times .1 = .01$, or 1% frequency of homozygotes) if the population is at Hardy-Weinberg equilibrium. To have a ~99% chance of identifying such alleles would require searching a population of 22 individuals (see Table below). If the major phenotypes are associated with heterozygous genotypes then we need to detect alleles present at ~.5% frequency ($2 \times .005 \times .995 = .00995$, or ~1% frequency of heterozygotes). A 99% chance of detecting such alleles would require ~40 individuals (Table below). Given the heterogeneity of the North American population we cannot assume that all genotypes are present in Hardy-Weinberg proportions, therefore a substantial oversampling may be done to increase the chances of detecting relevant variances: For our initial screening, usually, 62 individuals of known race/ethnicity are screened for variance. Variance detection studies can be extended to outliers for the phenotypes of interest to cover the possibility that important variances were missed in the normal population screening.

Allele frequencies	Number of subjects genotyped							
	n = 5	n = 10	n = 15	n = 20	n = 25	n = 30	n = 35	n = 50
p=.99,	9.56	18.21	26.03	33.10	39.50	45.28	50.52	63.40
p=.97,	26.26	45.62	59.90	70.43	78.19	83.92	88.14	95.24
p=.95,	40.13	64.15	78.53	87.15	92.30	95.39	97.24	99.65
p=.93,	51.60	76.58	88.66	94.51	97.34	98.71	99.38	99.93
p=.9, q =	65.13	87.84	95.76	98.52	99.48	99.82	99.94	>99.9
p=.8, q =	89.26	98.84	99.88	99.99	>99.9	>99.9	>99.9	>99.9
p=.7, q =	97.17	99.92	99.99	>99.9	>99.9	>99.9	>99.9	>99.9

Likelihood of Detecting Polymorphism in a Population as a Function of Allele Frequency & Number of Individuals Genotyped

The table above shows the probability (expressed as percent) of detecting both alleles (i.e. detecting heterozygotes) at a biallelic locus as a function of (i) the allele frequencies and (ii) the number of individuals genotyped. The chances of detecting heterozygotes increases as the frequencies of the two alleles approach 0.5 (down a column), and as the number of individuals genotyped increases (to the right along a row). The numbers in the table are given by the formula: $1 - (p)^{2n} - (q)^{2n}$. Allele frequencies are designated p and q and the number of individuals tested is designated n. (Since humans are diploid, the number of alleles tested is twice the number of individuals, or 2n.)

While it is preferable that numbers of individuals, or independent sequence samples, are screened to identify variances in a gene, it is also very beneficial to identify variances using smaller numbers of individuals or sequence samples. For example, even a comparison between the sequences of two samples or individuals can reveal sequence variances between them. Preferably, 5, 10, or more samples or individuals are screened.

Source of nucleic acid samples

Nucleic acid samples, for example for use in variance identification, can be obtained from a variety of sources as known to those skilled in the art, or can be obtained from genomic or cDNA sources by known methods. For example, the Coriell Cell Repository (Camden, N.J.) maintains over 6,000 human cell cultures, mostly fibroblast and lymphoblast cell lines comprising the NIGMS Human Genetic Mutant Cell Repository. A catalog (<http://locus.umdj.edu/nigms>) provides racial or ethnic identifiers for many of the cell lines. It is preferable to perform polymorphism discovery on a population that mimics the population to be evaluated in a clinical trial, both in terms of racial/ethnic/geographic background and in terms of disease status. Otherwise, it is generally preferable to include a broad population sample including, for example, (for trials in the United States): Caucasians of Northern, Central and Southern European origin, Africans or African-Americans, Hispanics or Mexicans, Chinese, Japanese, American Indian, East Indian, Arabs and Koreans.

Source of human DNA, RNA and cDNA samples

PCR based screening for DNA polymorphism can be carried out using either genomic DNA or cDNA produced from mRNA. For many genes, only cDNA sequences have been published, therefore the analysis of those genes is, at least initially, at the cDNA level since the determination of intron-exon boundaries and the isolation of flanking sequences is a laborious process. However, screening

genomic DNA has the advantage that variances can be identified in promoter, intron and flanking regions. Such variances may be biologically relevant. Therefore preferably, when variance analysis of patients with outlier responses is performed, analysis of selected loci at the genomic level is also performed. Such analysis would be contingent on the availability of a genomic sequence or intron-exon boundary sequences, and would also depend on the anticipated biological importance of the gene in connection with the particular response.

When cDNA is to be analyzed it is very beneficial to establish a tissue source in which the genes of interest are expressed at sufficient levels that cDNA can be readily produced by RT-PCR. Preliminary PCR optimization efforts for 19 of the 29 genes in Table 2 reveal that all 19 can be amplified from lymphoblastoid cell mRNA. The 7 untested genes belong on the same pathways and are expected to also be PCR amplifiable.

PCR Optimization

Primers for amplifying a particular sequence can be designed by methods known to those skilled in the art, including by the use of computer programs such as the PRIMER software available from Whitehead Institute/MIT Genome Center. In some cases it is preferable to optimize the amplification process according to parameters and methods known to those skilled in the art; optimization of PCR reactions based on a limited array of temperature, buffer and primer concentration conditions is utilized. New primers are obtained if optimization fails with a particular primer set.

Variance detection using T4 endonuclease VII mismatch cleavage method

Any of a variety of different methods for detecting variances in a particular gene can be utilized, such as those described in the patents and applications cited in section A above. An exemplary method is a T4 EndoVII method. The enzyme T4 endonuclease VII (T4E7) is derived from the bacteriophage T4. T4E7 specifically cleaves heteroduplex DNA containing single base mismatches, deletions or insertions. The site of cleavage is 1 to 6 nucleotides 3' of the mismatch. This activity has been exploited to develop a general method for detecting DNA sequence variances (Youil et al. 1995; Mashal and Sklar, 1995). A quality controlled T4E7 variance detection procedure based on the T4E7 patent of R.G.H. Cotton and co-workers. (Del Tito et al., in press) is preferably utilized. T4E7 has the advantages of being rapid, inexpensive, sensitive and selective. Further, since the enzyme

pinpoints the site of sequence variation, sequencing effort can be confined to a 25 - 30 nucleotide segment.

The major steps in identifying sequence variations in candidate genes using T4E7 are: (1) PCR amplify 400-600 bp segments from a panel of DNA samples; (2) mix a fluorescently-labeled probe DNA with the sample DNA; (3) heat and cool the samples to allow the formation of heteroduplexes; (4) add T4E7 enzyme to the samples and incubate for 30 minutes at 37°C, during which cleavage occurs at sequence variance mismatches; (5) run the samples on an ABI 377 sequencing apparatus to identify cleavage bands, which indicate the presence and location of variances in the sequence; (6) a subset of PCR fragments showing cleavage are sequenced to identify the exact location and identity of each variance.

The T4E7 Variance Imaging procedure has been used to screen particular genes. The efficiency of the T4E7 enzyme to recognize and cleave at all mismatches has been tested and reported in the literature. One group reported detection of 81 of 81 known mutations (Youil et al. 1995) while another group reported detection of 16 of 17 known mutations (Mashal and Sklar, 1995). Thus, the T4E7 method provides highly efficient variance detection.

DNA sequencing

A subset of the samples containing each unique T4E7 cleavage site is selected for sequencing. DNA sequencing can, for example, be performed on ABI 377 automated DNA sequencers using BigDye chemistry and cycle sequencing. Analysis of the sequencing runs will be limited to the 30-40 bases pinpointed by the T4E7 procedure as containing the variance. This provides the rapid identification of the altered base or bases.

In some cases, the presence of variances can be inferred from published articles which describe Restriction Fragment Length Polymorphisms (RFLP). The sequence variances or polymorphisms creating those RFLPs can be readily determined using convention techniques, for example in the following manner. If the RFLP was initially discovered by the hybridization of a cDNA, then the molecular sequence of the RFLP can be determined by restricting the cDNA probe into fragments and separately hybridizing to a Southern blot consisting of the restriction digestion with the enzyme which reveals the polymorphic site, identifying the sub-fragment which hybridizes to the polymorphic restriction fragment, obtaining a genomic clone of the gene (e.g., from commercial services such as Genome Systems (Saint Louis, Missouri) or Research Genetics (Alabama) which will provide appropriate genomic clones on receipt of appropriate primer pairs). Using the genomic clone, restrict the genomic clone with the restriction enzyme

which revealed the polymorphism and isolate the fragment which contains the polymorphism, e.g., identifying by hybridization to the cDNA which detected the polymorphism. The fragment is then sequenced across the polymorphic site. A copy of the other allele can be obtained by PCT from addition samples.

5 *Variance detection using sequence scanning*

In addition to the physical methods, e.g., those described above and others known to those skilled in the art (see, e.g., Housman, U.S. Patent 5,702,890; Housman et al., U.S. Patent Application 09/045,053), variances can be detected using computational methods, involving computer comparison of sequences from
10 two or more different biological sources, which can be obtained in various ways, for example from public sequence databases. The term "variance scanning" refers to a process of identifying sequence variances using computer-based comparison and analysis of multiple representations of at least a portion of one or more genes. Computational variance detection involves a process to distinguish true variances
15 from sequencing errors or other artifacts, and thus does not require perfectly accurate sequences. Such scanning can be performed in a variety of ways, preferably, for example, as described in Stanton et al., filed October 14, 1999, serial number 09/419,705, attorney docket number 246/128.

While the utilization of complete cDNA sequences is highly preferred, it is
20 also possible to utilize genomic sequences. Such analysis may be desired where the detection of variances in or near splice sites is sought. Such sequences may represent full or partial genomic DNA sequences for a gene or genes. Also, as previously indicated, partial cDNA sequences can also be utilized although this is less preferred. As described below, the variance scanning analysis can simply
25 utilize sequence overlap regions, even from partial sequences. Also, while the present description is provided by reference to DNA, e.g., cDNA, some sequences may be provided as RNA sequences, e.g., mRNA sequences. Such RNA sequences may be converted to the corresponding DNA sequences, or the analysis may use the RNA sequences directly.

30 B. Determination of Presence or Absence of Known Variances

The identification of the presence of previously identified variances in cells of an individual, usually a particular patient, can be performed by a number of different techniques as indicated in the Summary above. Such methods include
35 methods utilizing a probe which specifically recognizes the presence of a particular nucleic acid or amino acid sequence in a sample. Common types of probes include nucleic acid hybridization probes and antibodies, for example, monoclonal

antibodies, which can differentially bind to nucleic acid sequences differing in one or more variance sites or to polypeptides which differ in one or more amino acid residues as a result of the nucleic acid sequence variance or variances. Generation and use of such probes is well-known in the art and so is not described in detail
5 herein.

Preferably, however, the presence or absence of a variance is determined using nucleotide sequencing of a short sequence spanning a previously identified variance site. This will utilize validated genotyping assays for the polymorphisms previously identified. Since both normal and tumor cell genotypes can be measured,
10 and since tumor material will frequently only be available as paraffin embedded sections (from which RNA cannot be isolated), it will be necessary to utilize genotyping assays that will work on genomic DNA. Thus PCR reactions will be designed, optimized, and validated to accommodate the intron-exon structure of each of the genes. If the gene structure has been published (as it has for some of the
15 listed genes), PCR primers can be designed directly. However, if the gene structure is unknown, the PCR primers may need to be moved around in order to both span the variance and avoid exon-intron boundaries. In some cases one-sided PCR methods such as bubble PCR (Ausubel et al. 1997) may be useful to obtain flanking intronic DNA for sequence analysis.

20 Using such amplification procedures, the standard method used to genotype normal and tumor tissues will be DNA sequencing. PCR fragments encompassing the variances will be cycle sequenced on ABI 377 automated sequencers using Big Dye chemistry

25 C. Correlation of the Presence or Absence of Specific Variances with Differential Treatment Response

Prior to establishment of a diagnostic test for use in the selection of a treatment method or elimination of a treatment method, the presence or absence of one or more specific variances in a gene or in multiple genes is correlated with a
30 differential treatment response. (As discussed above, usually the existence of a variable response and the correlation of such a response to a particular gene is performed first.) Such a differential response can be determined using prospective and/or retrospective data. Thus, in some cases, published reports will indicate that the course of treatment will vary depending on the presence or absence of particular
35 variances. That information can be utilized to create a diagnostic test and/or incorporated in a treatment method as an efficacy or safety determination step.

Usually, however, the effect of one or more variances is separately determined. The determination can be performed by analyzing the presence or

absence of particular variances in patients who have previously been treated with a particular treatment method, and correlating the variance presence or absence with the observed course, outcome, and/or development of adverse events in those patients. This approach is useful in cases in which observation of treatment effects was clearly recorded and cell samples are available or can be obtained.

Alternatively, the analysis can be performed prospectively, where the presence or absence of the variance or variances in an individual is determined and the course, outcome, and/or development of adverse events in those patients is subsequently or concurrently observed and then correlated with the variance determination.

Analysis of Haplotypes Increases Power of Genetic Analysis

In some cases, variation in activity due to a single gene or a single genetic variance in a single gene may not be sufficient to account for a clinically significant fraction of the observed variation in patient response to a treatment, e.g., a drug, there may be other factors that account for some of the variation in patient response. Drug response phenotypes may vary continuously, and such (quantitative) traits may be influenced by a number of genes (Falconer and Mackay, Quantitative Genetics, 1997). Although it is impossible to determine *a priori* the number of genes influencing a quantitative trait, potentially only one or a few loci have large effects, where a large effect is 5-20% of total variation in the phenotype (Mackay, 1995).

Having identified genetic variation in enzymes that may affect action of a specific drug, it is useful to efficiently address its relation to phenotypic variation. The sequential testing for correlation between phenotypes of interest and single nucleotide polymorphisms may be adequate to detect associations if there are major effects associated with single nucleotide changes; certainly it is useful to this type of analysis. However there is no way to know in advance whether there are major phenotypic effects associated with single nucleotide changes and, even if there are, there is no way to be sure that the salient variance has been identified by screening cDNAs. A more powerful way to address the question of genotype-phenotype correlation is to assort genotypes into haplotypes. (A haplotype is the *cis* arrangement of polymorphic nucleotides on a particular chromosome.) Haplotype analysis has several advantages compared to the serial analysis of individual polymorphisms at a locus with multiple polymorphic sites.

(1) Of all the possible haplotypes at a locus (2^n haplotypes are theoretically possible at a locus with n binary polymorphic sites) only a small fraction will

generally occur at a significant frequency in human populations. Thus, association studies of haplotypes and phenotypes will involve testing fewer hypotheses. As a result there is a smaller probability of Type I errors, that is, false inferences that a particular variant is associated with a given phenotype.

(2) The biological effect of each variance at a locus may be different both in magnitude and direction. For example, a polymorphism in the 5' UTR may affect translational efficiency, a coding sequence polymorphism may affect protein activity, a polymorphism in the 3' UTR may affect mRNA folding and half life, and so on. Further, there may be interactions between variances: two neighboring polymorphic amino acids in the same domain - say cys/arg at residue 29 and met/val at residue 166 - may, when combined in one sequence, for example, 29cys-166val, have a deleterious effect, whereas 29cys-166met, 29arg-166met and 29arg-166val proteins may be nearly equal in activity. Haplotype analysis is the best method for assessing the interaction of variances at a locus.

(3) Templeton and colleagues have developed powerful methods for assorting haplotypes and analyzing haplotype/phenotype associations (Templeton et al., 1987). Alleles which share common ancestry are arranged into a tree structure (cladogram) according to their (inferred) time of origin in a population (that is, according to the principle of parsimony). Haplotypes that are evolutionarily ancient will be at the center of the branching structure and new ones (reflecting recent mutations) will be represented at the periphery, with the links representing intermediate steps in evolution. The cladogram defines which haplotype-phenotype association tests should be performed to most efficiently exploit the available degrees of freedom, focusing attention on those comparisons most likely to define functionally different haplotypes (Haviland et al., 1995). This type of analysis has been used to define interactions between heart disease and the apolipoprotein gene cluster (Haviland et al 1995) and Alzheimer's Disease and the Apo-E locus (Templeton 1995) among other studies, using populations as small as 50 to 100 individuals. The methods of Templeton have also been applied to measure the genetic determinants of variation in the angiotensin-I converting enzyme gene. (Keavney, B., McKenzie, C. A., Connoll, J.M.C., et al. Measured haplotype analysis of the angiotensin-I converting enzyme gene. *Human Molecular Genetics* 7: 1745-1751.)

Methods for determining haplotypes

The goal of haplotyping is to identify the common haplotypes at selected loci that have multiple sites of variance. Haplotypes are usually determined at the cDNA level. Several general approaches to identification of haplotypes can be employed. Haplotypes may also be estimated using computational methods or determined
5 definitively using experimental approaches. Computational approaches generally include an expectation maximization (E-M) algorithm (see, for example: Excoffier and Slatkin, *Mol. Biol. Evol.* 1995) or a combination of Parsimony (see below) and E-M methods.

Haplotypes can be determined experimentally without requirement of a
10 haplotyping method by genotyping samples from a set of pedigrees and observing the segregation of haplotypes. For example families collected by the Centre d'Etude du Polymorphisme Humaine (CEPH) can be used. Cell lines from these families are available from the Coriell Repository. This approach will be useful for cataloging common haplotypes and for validating methods on samples with known haplotypes.
15 The set of haplotypes determined by pedigree analysis can be useful in computational methods, including those utilizing the E-M algorithm.

Haplotypes can also be determined directly from cDNA using the T4E7 procedure. T4E7 cleaves mismatched heteroduplex DNA at the site of the mismatch. If a heteroduplex contains only one mismatch, cleavage will result in the
20 generation of two fragments. However, if a single heteroduplex (allele) contains two mismatches, cleavage will occur at two different sites resulting in the generation of three fragments. The appearance of a fragment whose size corresponds to the distance between the two cleavage sites is diagnostic of the two mismatches being present on the same strand (allele). Thus, T4E7 can be used to determine haplotypes
25 in diploid cells.

An alternative method, allele specific PCR, may be used for haplotyping. The utility of allele specific PCR for haplotyping has already been established (Michalatos-Beloin et al., 1996; Chang et al. 1997). Opposing PCR primers are
30 designed to cover two sites of variance (either adjacent sites or sites spanning one or more internal variances). Two versions of each primer are synthesized, identical to each other except for the 3' terminal nucleotide. The 3' terminal nucleotide is designed so that it will hybridize to one but not the other variant base. PCR amplification is then attempted with all four possible primer combinations in separate wells. Because Taq polymerase is very inefficient at extending 3'
35 mismatches, the only samples which will be amplified will be the ones in which the two primers are perfectly matched for sequences on the same strand (allele). The presence or absence of PCR product allows haplotyping of diploid cell lines. At

most two of four possible reactions should yield products. This procedure has been successfully applied, for example, to haplotype the DPD amino acid polymorphisms.

Parsimony methods are also useful for classifying DNA sequences, haplotypes or phenotypic characters. Parsimony principle maintains that the best explanation for the observed differences among sequences, phenotypes (individuals, species) etc., is provided by the smallest number of evolutionary changes.

Alternatively, simpler hypotheses are preferable to explain a set of data or patterns, than more complicated ones, and *ad hoc* hypotheses should be avoided whenever possible (Molecular Systematics, Hillis et al., 1996). Parsimony methods thus operate by minimizing the number of evolutionary steps or mutations (changes from one sequence/character) required to account for a given set of data.

For example, supposing we want to obtain relationships among a set of sequences and construct a structure (tree/topology), we first count the minimum number of mutations that are required for explaining the observed evolutionary changes among a set of sequences. A structure (topology) is constructed based on this number. When once this number is obtained, another structure is tried. This process is continued for all reasonable number of structures. Finally, the structure that required the smallest number of mutational steps is chosen as the likely structure/evolutionary tree for the sequences studied.

D. Selection of Treatment Method Using Variance Information

1. General

Once the presence or absence of a variance or variances in a gene or genes is shown to correlate with the efficacy or safety of a treatment method, that information can be used to select an appropriate treatment method for a particular patient. In the case of a treatment which is more likely to be effective when administered to a patient who has at least one copy of a gene with a particular variance or variances (in some cases the correlation with effective treatment is for patients who are homozygous for a variance or set of variances in a gene) than in patients with a different variance or set of variances, a method of treatment is selected (and/or a method of administration) which correlates positively with the particular variance presence or absence which provides the indication of effectiveness. As indicated in the Summary, such selection can involve a variety of different choices, and the correlation can involve a variety of different types of treatments, or choices of methods of treatment. In some cases, the selection may include choices between treatments or methods of administration where more than one method is likely to be effective, or where there is a range of expected effectiveness or different expected levels of contra-indication or deleterious effects.

In such cases the selection is preferably performed to select a treatment which will be as effective or more effective than other methods, while having a comparatively low level of deleterious effects. Similarly, where the selection is between method with differing levels of deleterious effects, preferably a method is selected which has low such effects but which is expected to be effective in the patient.

Alternatively, in cases where the presence or absence of the particular variance or variances is indicative that a treatment or method of administration is more likely to be ineffective or contra-indicated in a patient with that variance or variances, then such treatment or method of administration is generally eliminated for use in that patient.

2. Diagnostic Methods

Once a correlation between the presence and absence of at least one variance in a gene or genes and an indication of the effectiveness of a treatment, the determination of the presence or absence of that at least one variance provides diagnostic methods, which can be used as indicated in the Summary above to select methods of treatment, methods of administration of a treatment, methods of selecting a patient or patients for a treatment and others aspects in which the determination of the presence or absence of those variances provides useful information for selecting or designing or preparing methods or materials for medical use in the aspects of this invention. As previously stated, such variance determination or diagnostic methods can be performed in various ways as understood by those skilled in the art.

In certain variance determination methods, it is necessary or advantageous to amplify one or more nucleotide sequences in one or more of the genes identified herein. Such amplification can be performed by conventional methods, e.g., using polymerase chain reaction (PCR) amplification. Such amplification methods are well-known to those skilled in the art and will not be specifically described herein. For most applications relevant to the present invention, a sequence to be amplified includes at least one variance site, which is preferably a site or sites which provide variance information indicative of the effectiveness of a method of treatment or method of administration of a treatment, or effectiveness of a second method of treatment which reduces a deleterious effect of a first treatment method, or which enhances the effectiveness of a first method of treatment. Thus, for PCR, such amplification generally utilizes primer oligonucleotides which bind to or extend through at least one such variance site under amplification conditions.

For convenient use of the amplified sequence, e.g., for sequencing, it is beneficial that the amplified sequence be of limited length, but still long enough to

allow convenient and specific amplification. Thus, preferably the amplified sequence has a length as described in the Summary.

Also, in certain variance determination, it is useful to sequence one or more portions of a gene or genes, in particular, portions of the genes identified in this disclosure. As understood by persons familiar with nucleic acid sequencing, there are a variety of effective methods. In particular, sequencing can utilize dye termination methods and mass spectrometric methods. The sequencing generally involves a nucleic acid sequence which includes a variance site as indicated above in connection with amplification. Such sequencing can directly provide determination of the presence or absence of a particular variance or set of variances, e.g., a haplotype, by inspection of the sequence (visually or by computer). Such sequencing is generally conducted on PCR amplified sequences in order to provide sufficient signal for practical or reliable sequence determination.

Likewise, in certain variance determinations, it is useful to utilize a probe or probes. As previously described, such probes can be of a variety of different types.

VII. Loss of Heterozygosity and Conditionally Essential Genes

Different environmental, pharmacological, and physical changes in the environment that result in homeostatic or compensatory responses in which genes that are not normally essential for cell survival or proliferation become essential are known in the art.

When LOH results in a difference in normal cell genotype vs. cancer cell genotype that affects a locus encoding a product affecting the cells' ability to survive in the presence of an environmental change, or a pharmaceutical or biological agent, or a physical factor, there is an opportunity to exploit a therapeutic window between cancer cells and normal cells. Below we describe specific examples of genes that (1) affect cell responses to altered environments, (2) are located on chromosomes that undergo LOH in cancer and (3) exist in two or more variant forms. These examples have been selected to illustrate how the therapeutic strategy described in this application would work with a variety of different alterations in chemical or physical environment. Example 20 describes a gene (Dihydropyrimidine Dehydrogenase) that mediates response to an altered chemical environment (presence of the toxic chemical 5-fluorouridine) by specifically transforming the chemical to an inactive metabolite. Example 27 describes a gene (Methylguanine methyltransferase) that mediates response to an altered chemical environment (presence of toxic chemicals such as nitrosourea or other alkylating agents) by removing methyl or alkyl adducts to DNA, the principal toxic lesion of these agents.

Example 21 describes a set of genes (Fanconi Anemia genes A,B,C,D,E,F,G and H) which mediate response to an altered chemical environment (presence of chemicals which cause DNA crosslinking, such as diepoxybutane, mitomycin C and cisplatinum) by repairing the crosslinks. Example 25 describes a set of genes (the DNA Dependent Protein Kinase Complex, including the DNA Dependent Protein Kinase catalytic subunit (DNA-PKcs), the DNA binding component (called Ku), made up of Ku-70 and Ku-86 kDa subunits, and the Ku-86 related protein Karp-1) that mediates repair of double stranded DNA breaks, such as occurs after x-irradiation. Example 22 describes a gene (asparagine synthase) that mediates response to an altered nutritional environment (absence of extracellular asparagine) which can be produced by an enzyme such as asparaginase, which hydrolyzes serum asparagine. Example 26 describes the Ataxia Telangiectasia gene, which is involved in response to ionizing radiation and radiomimetic chemicals. Other detailed examples include methionine synthase (Ex. 23) and methylthioadenosine phosphorylase (Ex. 24). Other examples include Poly (ADP) Ribose Polymerase (PARP), Glutathione-S- Transferase pi (GST-pi), NF-kappa B, Abl Kinase, 3-alkylguanine alkyltransferase, N-methylpurine DNA glycosylase (hydrolyzes the deoxyribose N-glycosidic bond to excise 3-methyladenine and 7-methylguanine from alkylating agent-damaged DNA polymers), OGG-1, MDR-1.

In addition to the direct use of conditionally essential (or essential) genes in allele-specific inhibitor applications, the information provided by the LOH status of a gene. For example, in some cases, the effect of LOH can be a gene dosage effect. This can additionally be combined with a reduced activity associated with particular forms of the gene. Either or both types of information can be used to identify patients who would be expected to respond differently to a treatment targeting that gene than would patients with two copies of the gene, or with at least one copy of a different form of the gene than remained after LOH. To illustrate, a patient may be heterozygous for a high activity allele and a low activity allele. LOH in cancer cells could remove either the high activity allele or the low activity allele, leaving only the other allele in cancer cells in the patient, while the normal cells would have intermediate activity due the presence of both alleles. As a result, a therapy targeting or otherwise involving that gene in the response to treatment would be expected to result in variation in response between the normal cells and the cancer cells in the patient. If the low activity allele correlated with high response to the therapy, then it would be expected that the anti-cancer treatment would be more effective in a patient with such LOH than in a patient in whom cancer cells had not undergone LOH with respect to that gene.

Indeed, LOH assays for particular genes can also be used as surrogate assays for other LOH of other genes located near the marker gene. Thus, the marker gene can, for example, be used in connection with LOH-related effects or evaluations of other nearby genes. Such genes can include genes in the same pathway, as those genes are often located in close proximity on the same chromosome.

It has been shown that LOH at tumor suppressor genes correlates with anticancer chemotherapy response. Thus, LOH information on tumor suppressor genes can also be used in connection with LOH and/or pharmacogenetic information about other genes. As a result, it is beneficial to determine both the LOH status of the tumor suppressor gene or genes and one or more additional genes.

Together, or separately, the LOH information and the variance-based pharmacogenetic information can be used to identify patient subset that will respond differently to a particular therapy related to particular genes and/or to select appropriate therapies for patients based on the forms of the gene or genes in disease cells and normal cells.

VII. Pharmaceutical Compositions, Including Pharmaceutical Compositions Adapted to be Preferentially Effective in Patients Having Particular Genetic Characteristics

A. General

The methods of the present invention, in many cases will utilize conventional pharmaceutical compositions, but will allow more advantageous and beneficial use of those compositions due to the ability to identify patients who are likely to benefit from a particular treatment or to identify patients for whom a particular treatment is less likely to be effective or for whom a particular treatment is likely to produce undesirable or intolerable effects. However, in some cases, it is advantageous to utilize compositions which are adapted to be preferentially effective in patients who possess particular genetic characteristics, i.e., in whom a particular variance or variances in one or more genes is present or absent (depending on whether the presence or the absence of the variance or variances in a patient is correlated with an increased expectation of beneficial response). Thus, for example, the presence of a particular variance or variances may indicate that a patient can beneficially receive a significantly higher dosage of a drug than a patient having a different

B. Regulatory Indications and Restrictions

The sale and use of drugs and the use of other treatment methods usually are subject to certain restrictions by a government regulatory agency charged with

ensuring the safety and efficacy of drugs and treatment methods for medical use, and approval is based on particular indications. In the present invention it is found that variability in patient response or patient tolerance of a drug or other treatment often correlates with the presence or absence of particular variances in particular genes.

5 Thus, it is expected that such a regulatory agency may indicate that the approved indications for use of a drug with a variance-related variable response or toleration include use only in patients in whom the drug will be effective, and/or for whom the administration of the drug will not have intolerable deleterious effects, such as excessive toxicity or unacceptable side-effects. Conversely, the drug may be given
10 for an indication that it may be used in the treatment of a particular disease or condition where the patient has at least one copy of a particular variance, variances, or variant form of a gene. Even if the approved indications are not narrowed to such groups, the regulatory agency may suggest use limited to particular groups or excluding particular groups or may state advantages of use or exclusion of such
15 groups or may state a warning on the use of the drug in certain groups. Consistent with such suggestions and indications, such an agency may suggest or recommend the use of a diagnostic test to identify the presence or absence of the relevant variances in the prospective patient. Such diagnostic methods are described in this description. Generally, such regulatory suggestion or indication is provided in a
20 product insert or label, and is generally reproduced in references such as the Physician's Desk Reference (PDR). Thus, this invention also includes drugs or pharmaceutical compositions which carry such a suggestion or statement of indication or warning or suggestion for a diagnostic test, and which may also be packaged with an insert or label stating the suggestion or indication or warning or
25 suggestion for a diagnostic test.

In accord with the possible variable treatment responses, an indication or suggestion can specify that a patient be heterozygous, or alternatively, homozygous for a particular variance or variances or variant form of a gene. Alternatively, an indication or suggestion may specify that a patient have no more than one copy, or
30 zero copies, of a particular variance, variances, or variant form of a gene.

A regulatory indication or suggestion may concern the variances or variant forms of a gene in normal cells of a patient and/or in cells involved in the disease or condition. For example, in the case of a cancer treatment, the response of the cancer cells can depend on the form of a gene remaining in cancer cells following loss of
35 heterozygosity affecting that gene. Thus, even though normal cells of the patient may contain a form of the gene which correlates with effective treatment response, the absence of that form in cancer cells will mean that the treatment would be less likely to be effective in that patient than in another patient who retained in cancer

cells the form of the gene which correlated with effective treatment response. Those skilled in the art will understand whether the variances or gene forms in normal or disease cells are most indicative of the expected treatment response, and will generally utilize a diagnostic test with respect to the appropriate cells. Such a cell type indication or suggestion may also be contained in a regulatory statement, e.g., on a label or in a product insert.

C. Preparation and Administration of Drugs and Pharmaceutical Compositions Including Pharmaceutical Compositions Adapted to be Preferentially Effective in Patients Having Particular Genetic Characteristics

A particular compound useful in this invention can be administered to a patient either by itself, or in pharmaceutical compositions where it is mixed with suitable carriers or excipient(s). In treating a patient exhibiting a disorder of interest, a therapeutically effective amount of a agent or agents such as these is administered. A therapeutically effective dose refers to that amount of the compound that results in amelioration of one or more symptoms or a prolongation of survival in a patient.

Toxicity and therapeutic efficacy of such compounds can be determined by standard pharmaceutical procedures in cell cultures or experimental animals, e.g., for determining the LD₅₀ (the dose lethal to 50% of the population) and the ED₅₀ (the dose therapeutically effective in 50% of the population). The dose ratio between toxic and therapeutic effects is the therapeutic index and it can be expressed as the ratio LD₅₀/ED₅₀. Compounds which exhibit large therapeutic indices are preferred. The data obtained from these cell culture assays and animal studies can be used in formulating a range of dosage for use in human. The dosage of such compounds lies preferably within a range of circulating concentrations that include the ED₅₀ with little or no toxicity. The dosage may vary within this range depending upon the dosage form employed and the route of administration utilized.

For any compound used in the method of the invention, the therapeutically effective dose can be estimated initially from cell culture assays. For example, a dose can be formulated in animal models to achieve a circulating plasma concentration range that includes the IC₅₀ as determined in cell culture. Such information can be used to more accurately determine useful doses in humans. Levels in plasma may be measured, for example, by HPLC.

The exact formulation, route of administration and dosage can be chosen by the individual physician in view of the patient's condition. (See e.g. Fingl et. al., in The Pharmacological Basis of Therapeutics, 1975, Ch. 1 p.1). It should be noted that the attending physician would know how to and when to terminate, interrupt, or adjust administration due to toxicity, or to organ dysfunctions. Conversely, the

attending physician would also know to adjust treatment to higher levels if the clinical response were not adequate (precluding toxicity). The magnitude of an administered dose in the management of disorder of interest will vary with the severity of the condition to be treated and the route of administration. The severity
5 of the condition may, for example, be evaluated, in part, by standard prognostic evaluation methods. Further, the dose and perhaps dose frequency, will also vary according to the age, body weight, and response of the individual patient. A program comparable to that discussed above may be used in veterinary medicine.

Depending on the specific conditions being treated, such agents may be
10 formulated and administered systemically or locally. Techniques for formulation and administration may be found in Remington's Pharmaceutical Sciences, 18th ed., Mack Publishing Co., Easton, PA (1990). Suitable routes may include oral, rectal, transdermal, vaginal, transmucosal, or intestinal administration; parenteral delivery, including intramuscular, subcutaneous, intramedullary injections, as well as
15 intrathecal, direct intraventricular, intravenous, intraperitoneal, intranasal, or intraocular injections, just to name a few.

For injection, the agents of the invention may be formulated in aqueous solutions, preferably in physiologically compatible buffers such as Hanks's solution, Ringer's solution, or physiological saline buffer. For such transmucosal
20 administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art.

Use of pharmaceutically acceptable carriers to formulate the compounds herein disclosed for the practice of the invention into dosages suitable for systemic administration is within the scope of the invention. With proper choice of carrier
25 and suitable manufacturing practice, the compositions of the present invention, in particular, those formulated as solutions, may be administered parenterally, such as by intravenous injection. The compounds can be formulated readily using pharmaceutically acceptable carriers well known in the art into dosages suitable for oral administration. Such carriers enable the compounds of the invention to be
30 formulated as tablets, pills, capsules, liquids, gels, syrups, slurries, suspensions and the like, for oral ingestion by a patient to be treated.

Agents intended to be administered intracellularly may be administered using techniques well known to those of ordinary skill in the art. For example, such agents may be encapsulated into liposomes, then administered as described above.

35 Liposomes are spherical lipid bilayers with aqueous interiors. All molecules present in an aqueous solution at the time of liposome formation are incorporated into the aqueous interior. The liposomal contents are both protected from the external microenvironment and, because liposomes fuse with cell membranes, are efficiently

delivered into the cell cytoplasm. Additionally, due to their hydrophobicity, small organic molecules may be directly administered intracellularly.

Pharmaceutical compositions suitable for use in the present invention include compositions wherein the active ingredients are contained in an effective amount to achieve its intended purpose. Determination of the effective amounts is well within the capability of those skilled in the art, especially in light of the detailed disclosure provided herein. In addition to the active ingredients, these pharmaceutical compositions may contain suitable pharmaceutically acceptable carriers comprising excipients and auxiliaries which facilitate processing of the active compounds into preparations which can be used pharmaceutically. The preparations formulated for oral administration may be in the form of tablets, dragees, capsules, or solutions. The pharmaceutical compositions of the present invention may be manufactured in a manner that is itself known, *e.g.*, by means of conventional mixing, dissolving, granulating, dragee-making, levitating, emulsifying, encapsulating, entrapping or lyophilizing processes.

Pharmaceutical formulations for parenteral administration include aqueous solutions of the active compounds in water-soluble form. Additionally, suspensions of the active compounds may be prepared as appropriate oily injection suspensions. Suitable lipophilic solvents or vehicles include fatty oils such as sesame oil, or synthetic fatty acid esters, such as ethyl oleate or triglycerides, or liposomes. Aqueous injection suspensions may contain substances which increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran. Optionally, the suspension may also contain suitable stabilizers or agents which increase the solubility of the compounds to allow for the preparation of highly concentrated solutions.

Pharmaceutical preparations for oral use can be obtained by combining the active compounds with solid excipient, optionally grinding a resulting mixture, and processing the mixture of granules, after adding suitable auxiliaries, if desired, to obtain tablets or dragee cores. Suitable excipients are, in particular, fillers such as sugars, including lactose, sucrose, mannitol, or sorbitol; cellulose preparations such as, for example, maize starch, wheat starch, rice starch, potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropylmethyl-cellulose, sodium carboxymethylcellulose, and/or polyvinylpyrrolidone (PVP). If desired, disintegrating agents may be added, such as the cross-linked polyvinyl pyrrolidone, agar, or alginic acid or a salt thereof such as sodium alginate. Dragee cores are provided with suitable coatings. For this purpose, concentrated sugar solutions may be used, which may optionally contain gum arabic, talc, polyvinyl pyrrolidone, carbopol gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and

suitable organic solvents or solvent mixtures. Dyestuffs or pigments may be added to the tablets or dragee coatings for identification or to characterize different combinations of active compound doses.

Pharmaceutical preparations which can be used orally include push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a plasticizer, such as glycerol or sorbitol. The push-fit capsules can contain the active ingredients in admixture with filler such as lactose, binders such as starches, and/or lubricants such as talc or magnesium stearate and, optionally, stabilizers. In soft capsules, the active compounds may be dissolved or suspended in suitable liquids, such as fatty oils, liquid paraffin, or liquid polyethylene glycols. In addition, stabilizers may be added.

The invention described herein features methods for determining the appropriate identification of a patient diagnosed with a neurological disease or neurological dysfunction based on an analysis of the patient's allele status for a gene listed in Tables 1-6, 12-17, and 18-23. Specifically, the presence of at least one allele indicates that a patient will respond to a candidate therapeutic intervention aimed at treating clinical symptoms. In a preferred approach, the patient's allele status is rapidly diagnosed using a sensitive PCR assay and a treatment protocol is rendered. The invention also provides a method for forecasting patient outcome and the suitability of the patient for entering a clinical drug trial for the testing of a candidate therapeutic intervention for a disease, condition, or dysfunction as identified herein.

The findings described herein indicate the predictive value of the target allele in identifying patients at risk for a disease or disorder as identified for aspects herein. In addition, because the underlying mechanism influenced by the allele status is not disease-specific, the allele status is suitable for making patient predictions for diseases not affected by the pathway as well.

The following examples, which describe exemplary techniques and experimental results, are provided for the purpose of illustrating the invention, and should not be construed as limiting.

Example 1

Method for Producing cDNA

In order to identify sequence variances in a gene by laboratory methods it is in some instances useful to produce cDNA(s) from multiple human subjects. (In other instances it may be preferable to study genomic DNA.). Methods for producing cDNA are known to those skilled in the art, as are methods for amplifying and sequencing the cDNA or portions thereof. An example of a useful cDNA

production protocol is provided below. As recognized by those skilled in the art, other specific protocols can also be used.

cDNA Production

** Make sure that all tubes and pipette tips are RNase-free. (Bake them overnight at 100°C in a vacuum oven to make them RNase-free.)

1. Add the following to a RNase-free 0.2 ml micro-amp tube and mix gently:

24 ul water (DEPC treated)
12 ul RNA (1ug/ul)
12 ul random hexamers(50 ng/ul)

2. Heat the mixture to 70°C for ten minutes.

3. Incubate on ice for 1 minute.

4. Add the following:

16 ul 5 X Synthesis Buffer
8 ul 0.1 M DTT
4 ul 10 mM dNTP mix (10 mM each dNTP)
4 ul SuperScript RT II enzyme

Pipette gently to mix.

5. Incubate at 42°C for 50 minutes.

6. Heat to 70°C for ten minutes to kill the enzyme, then place it on ice.

7. Add 160 ul of water to the reaction so that the final volume is 240 ul.

8. Use PCR to check the quality of the cDNA. Use primer pairs that will give a ~800 base pair long piece. See "PCR Optimization" for the PCR protocol.

The following chart shows the reagent amounts for a 20 ul reaction, a 80 ul reaction, and a batch of 39 (which makes enough mix for 36) reactions:

	20 ul X 1 tube	80 ul X 1 tube	80ul X 39 tubes	
--	----------------	----------------	-----------------	--

Water	6 ul	24 ul	936	water
RNA	3 ul	12 ul		RNA
random hexamers	3 ul	12 ul	468	random hexamers
synthesis buffer	4 ul	16 ul	624	synthesis buffer
0.1 M DTT	2 ul	8 ul	312	0.1 M DTT
10mM dNTP	1 ul	4 ul	156	10mM dNTP
SSRT	1 ul	4 ul	156	SSRT

Example 2

Method for Detecting Variances by Single Strand Conformation Polymorphism (SSCP) Analysis

This example describes the SSCP technique for identification of sequence variances of genes. SSCP is usually paired with a DNA sequencing method, since the SSCP method does not provide the nucleotide identity of variances. One useful sequencing method, for example, is DNA cycle sequencing of ^{32}P labeled PCR products using the Femtomole DNA cycle sequencing kit from Promega (WI) and the instructions provided with the kit. Fragments are selected for DNA sequencing based on their behavior in the SSCP assay.

Single strand conformation polymorphism screening is a widely used technique for identifying and discriminating DNA fragments which differ from each other by as little as a single nucleotide. As originally developed by Orita et al. (Detection of polymorphisms of human DNA by gel electrophoresis as single-strand conformation polymorphisms. *Proc Natl Acad Sci U S A.* 86(8):2766-70, 1989), the technique was used on genomic DNA, however the same group showed that the technique works very well on PCR amplified DNA as well. In the last 10 years the technique has been used in hundreds of published papers, and modifications of the technique have been described in dozens of papers. The enduring popularity of the technique is due to (1) a high degree of sensitivity to single base differences (>90%) (2) a high degree of selectivity, measured as a low frequency of false positives, and (3) technical ease. SSCP is almost always used together with DNA sequencing because SSCP does not directly provide the sequence basis of differential fragment mobility. The basic steps of the SSCP procedure are described below.

When the intent of SSCP screening is to identify a large number of gene variances it is useful to screen a relatively large number of individuals of different racial, ethnic and/or geographic origins. For example, 32 or 48 or 96 individuals is a convenient number to screen because gel electrophoresis apparatus are available with 96 wells (Applied Biosystems Division of Perkin Elmer Corporation), allowing 3 X 32, 2 X 48 or 96 samples to be loaded per gel.

The 32 (or more) individuals screened should be representative of most of the worlds major populations. For example, an equal distribution of Africans, Europeans and Asians constitutes a reasonable screening set. One useful source of cell lines from different populations is the Coriell Cell Repository (Camden, NJ), which sells EBV immortalized lymphoblastoid cells obtained from several thousand subjects, and includes the racial/ethnic/geographic background of cell line donors in its catalog. Alternatively, a panel of cDNAs can be isolated from any specific target population.

SSCP can be used to analyze cDNAs or genomic DNAs. For many genes cDNA analysis is preferable because for many genes the full genomic sequence of the target gene is not available, however, this circumstance will change over the next few years. To produce cDNA requires RNA. Therefore each cell lines is grown to mass culture and RNA is isolated using an acid/phenol protocol, sold in kit form as Trizol by Life Technologies (Gaithersburg, MD). The unfractionated RNA is used to produce cDNA by the action of a modified Maloney Murine Leukemia Virus Reverse Transcriptase, purchased in kit form from Life Technologies (Superscript II kit). The reverse transcriptase is primed with random hexamer primers to initiate cDNA synthesis along the whole length of the RNAs. This proved useful later in obtaining good PCR products from the 5' ends of some genes. Alternatively, oligodT can be used to prime cDNA synthesis.

Material for SSCP analysis can be prepared by PCR amplification of the cDNA in the presence of one α ^{32}P labeled dNTP (usually α ^{32}P dCTP). Usually the concentration of nonradioactive dCTP is dropped from 200 μM (the standard concentration for each of the four dNTPs) to about 100 μM , and ^{32}P dCTP is added to a concentration of about 0.1-0.3 μM . This involves adding a 0.3- 1 μl (3-10 μCi) of ^{32}P cCTP to a 10 μl PCR reaction. Radioactive nucleotides can be purchased from DuPont/New England Nuclear.

The customary practice is to amplify about 200 base pair PCR products for SSCP, however, an alternative approach is to amplify about 0.8-1.4 kb fragments and then use several cocktails of restriction endonucleases to digest those into smaller fragments of about 0.1-0.4kb, aiming to have as many fragments as possible between .15 and .3 kb. The digestion strategy has the advantage that less PCR is required, reducing both time and costs. Also, several different restriction enzyme digests can be performed on each set of samples (for example 96 cDNAs), and then each of the digests can be run separately on SSCP gels. This redundant method (where each nucleotide is surveyed in three different fragments) reduces both the false negative and false positive rates. For example: a site of variance might lie within 2 bases of the end of a fragment in one digest, and as a result not affect the

conformation of that strand; the same variance, in a second or third digest, would likely lie in a location more prone to affect strand folding, and therefore be detected by SSCP.

After digestion, the radiolabelled PCR products are diluted 1:5 by adding
5 formamide load buffer (80% formamide, 1X SSCP gel buffer) and then denatured by heating to 90°C for 10 minutes, and then allowed to renature by quickly chilling on ice. This procedure (both the dilution and the quick chilling) promotes intra- (rather than inter-) strand association and secondary structure formation. The secondary
10 structure of the single strands influences their mobility on nondenaturing gels, presumably by influencing the number of collisions between the molecule and the gel matrix (i.e., gel sieving). Even single base differences consistently produce changes in intrastrand folding sufficient to register as mobility differences on SSCP.

The single strands were then resolved on two gels, one a 5.5% acrylamide, 0.5X TBE gel, the other an 8% acrylamide, 10% glycerol, 1X TTE gel. (Other gel
15 recipes are known to those skilled in the art.) The use of two gels provides a greater opportunity to recognize mobility differences. Both glycerol and acrylamide concentration have been shown to influence SSCP performance. By routinely analyzing three different digests under two gel conditions (effectively 6 conditions), and by looking at both strands under all 6 conditions, one can achieve a 12-fold
20 sampling of each base pair of cDNA. However, if the goal is to rapidly survey many genes or cDNAs then a less redundant procedure would be optimal.

Example 3**Method for Detecting Variances by T4 endonuclease VII (T4E7) mismatch cleavage method**

The enzyme T4 endonuclease VII is derived from the bacteriophage T4. T4 endonuclease VII is used by the bacteriophage to cleave branched DNA intermediates which form during replication so the DNA can be processed and packaged. T4 endonuclease can also recognize and cleave heteroduplex DNA containing single base mismatches as well as deletions and insertions. This activity of the T4 endonuclease VII enzyme can be exploited to detect sequence variances present in the general population.

The following are the major steps involved in identifying sequence variations in a candidate gene by T4 endonuclease VII mismatch cleavage:

1. Amplification by the polymerase chain reaction (PCR) of 400-600 bp regions of the candidate gene from a panel of DNA samples. The DNA samples can either be cDNA or genomic DNA and will represent some cross section of the world population.
2. Mixing of a fluorescently labeled probe DNA with the sample DNA. Heating and cooling the mixtures causing heteroduplex formation between the probe DNA and the sample DNA.
3. Addition of T4 endonuclease VII to the heteroduplex DNA samples. T4 endonuclease will recognize and cleave at sequence variance mismatches formed in the heteroduplex DNA.
4. Electrophoresis of the cleaved fragments on an ABI sequencer to determine the site of cleavage.
5. Sequencing of a subset of PCR fragments identified by T4 endonuclease VI to contain variances to establish the specific base variation at that location.

A more detailed description of the procedure is as follows:

A candidate gene sequence is downloaded from an appropriate database. Primers for PCR amplification are designed which will result in the target sequence being divided into amplification products of between 400 and 600 bp. There will be a minimum of a 50 bp of overlap not including the primer sequences between the 5' and 3' ends of adjacent fragments to ensure the detection of variances which are located close to one of the primers.

Optimal PCR conditions for each of the primer pairs is determined experimentally. Parameters including but not limited to annealing temperature, pH, MgCl₂ concentration, and KCl concentration will be varied until conditions for optimal PCR amplification are established. The PCR conditions derived for each

primer pair is then used to amplify a panel of DNA samples (cDNA or genomic DNA) which is chosen to best represent the various ethnic backgrounds of the world population or some designated subset of that population.

One of the DNA samples is chosen to be used as a probe. The same PCR
5 conditions used to amplify the panel are used to amplify the probe DNA. However, a fluorescently labeled nucleotide is included in the deoxy-nucleotide mix so that a percentage of the incorporated nucleotides will be fluorescently labeled.

The labeled probe is mixed with the corresponding PCR products from each
10 of the DNA samples and then heated and cooled rapidly. This allows the formation of heteroduplexes between the probe and the PCR fragments from each of the DNA samples. T4 endonuclease VII is added directly to these reactions and allowed to incubate for 30 min. at 37 C. 10 ul of the Formamide loading buffer is added directly to each of the samples and then denatured by heating and cooling. A
15 portion of each of these samples is electrophoresed on an ABI 377 sequencer. If there is a sequence variance between the probe DNA and the sample DNA a mismatch will be present in the heteroduplex fragment formed. The enzyme T4 endonuclease VII will recognize the mismatch and cleave at the site of the mismatch. This will result in the appearance of two peaks corresponding to the two
20 cleavage products when run on the ABI 377 sequencer.

Fragments identified as containing sequencing variances are subsequently
sequenced using conventional methods to establish the exact location and sequence
variance.

Example 4**Method for Detecting Variances by DNA sequencing.**

Sequencing by the Sanger dideoxy method or the Maxim Gilbert chemical cleavage method is widely used to determine the nucleotide sequence of genes. Presently, a worldwide effort is being put forward to sequence the entire human genome. The Human Genome Project as it is called has already resulted in the identification and sequencing of many new human genes. Sequencing can not only be used to identify new genes, but can also be used to identify variations between individuals in the sequence of those genes.

The following are the major steps involved in identifying sequence variations in a candidate gene by sequencing:

1. Amplification by the polymerase chain reaction (PCR) of 400-700 bp regions of the candidate gene from a panel of DNA samples. The DNA samples can either be cDNA or genomic DNA and will represent some cross section of the world population.
2. Sequencing of the resulting PCR fragments using the Sanger dideoxy method. Sequencing reactions are performed using fluorescently labeled dideoxy terminators and fragments are separated by electrophoresis on an ABI 377 sequencer or its equivalent.
3. Analysis of the resulting data from the ABI 377 sequencer using software programs designed to identify sequence variations between the different samples analyzed.

A more detailed description of the procedure is as follows:

A candidate gene sequence is downloaded from an appropriate database. Primers for PCR amplification are designed which will result in the target sequence being divided into amplification products of between 400 and 700 bp. There will be a minimum of a 50 bp of overlap not including the primer sequences between the 5' and 3' ends of adjacent fragments to ensure the detection of variances which are located close to one of the primers.

Optimal PCR conditions for each of the primer pairs is determined experimentally. Parameters including but not limited to annealing temperature, pH, MgCl₂ concentration, and KCl concentration will be varied until conditions for optimal PCR amplification are established. The PCR conditions derived for each primer pair is then used to amplify a panel of DNA samples (cDNA or genomic

DNA) which is chosen to best represent the various ethnic backgrounds of the world population or some designated subset of that population.

PCR reactions are purified using the QIAquick 8 PCR purification kit (Qiagen cat# 28142) to remove nucleotides, proteins and buffers. The PCR reactions are mixed with 5 volumes of Buffer PB and applied to the wells of the QIAquick strips. The liquid is pulled through the strips by applying a vacuum. The wells are then washed two times with 1 ml of buffer PE and allowed to dry for 5 minutes under vacuum. The PCR products are eluted from the strips using 60 ul of elution buffer.

The purified PCR fragments are sequenced in both directions using the Perkin Elmer ABI Prism™ Big Dye™ terminator Cycle Sequencing Ready Reaction Kit (Cat# 4303150). The following sequencing reaction is set up: 8.0 ul Terminator Ready Reaction Mix, 6.0 ul of purified PCR fragment, 20 picomoles of primer, deionized water to 20 ul. The reactions are run through the following cycles 25 times: 96°C for 10 second, annealing temperature for that particular PCR product for 5 seconds, 60°C for 4 minutes.

The above sequencing reactions are ethanol precipitated directly in the PCR plate, washed with 70% ethanol, and brought up in a volume of 6 ul of formamide dye. The reactions are heated to 90°C for 2 minutes and then quickly cooled to 4°C. 1 ul of each sequencing reaction is then loaded and run on an ABI 377 sequencer.

The output for the ABI sequencer appears as a series of peaks where each of the different nucleotides. A, C, G, and T appear as a different color. The nucleotide at each position in the sequence is determined by the most prominent peak at each location. Comparison of each of the sequencing outputs for each sample can be examined using software programs to determine the presence of a variance in the sequence. One example of heterozygote detection using sequencing with dye labeled terminators is described by Kwok *et. al.* (Kwok, P.-Y.; Carlson, C.; Yager, T.D., Ankener, W., and D. A. Nickerson, *Genomics* 23, 138-144, 1994). The software compares each of the normalized peaks between all the samples base by base and looks for a 40% decrease in peak height and the concomitant appearance of a new peak underneath. Possible variances flagged by the software are further analyzed visually to confirm their validity.

Example 5**Hardy-Weinberg equilibrium**

Evolution is the process of change and diversification of organisms through time, and evolutionary change affects morphology, physiology and reproduction of organisms, including humans. These evolutionary changes are the result of changes in the underlying genetic or hereditary material. Evolutionary changes in a group of interbreeding individuals or Mendelian population, or simply populations, are described in terms of changes in the frequency of genotypes and their constituent alleles. Genotype frequencies for any given generation is the result of the mating among members (genotypes) of their previous generation. Thus, the expected proportion of genotypes from a random union of individuals in a given population is essential for describing the total genetic variation for a population of any species. For example, the expected number of genotypes that could form from the random union of two alleles, A and a, of a gene are AA, Aa and aa. The expected frequency of genotypes in a large, random mating population was discovered to remain constant from generation to generation; or achieve Hardy-Weinberg equilibrium, named after its discoverers. The expected genotypic frequencies of alleles A and a (AA, 2Aa, aa) are conventionally described in terms of $p^2 + 2pq + q^2$ in which p and q are the allele frequencies of A and a. In this equation ($p^2 + 2pq + q^2 = 1$), p is defined as the frequency of one allele and q as the frequency of another allele for a trait controlled by a pair of alleles (A and a). In other words, p equals all of the alleles in individuals who are homozygous dominant (AA) and half of the alleles in individuals who are heterozygous (Aa) for this trait. In mathematical terms, this is

$$p = AA + \frac{1}{2}Aa$$

Likewise, q equals the other half of the alleles for the trait in the population, or

$$q = aa + \frac{1}{2}Aa$$

Because there are only two alleles in this case, the frequency of one plus the frequency of the other must equal 100%, which is to say

$$p + q = 1$$

Alternatively,

$$p = 1 - q \text{ OR } q = 1 - p$$

All possible combinations of two alleles can be expressed as:

$$(p + q)^2 = 1$$

or more simply,

$$p^2 + 2pq + q^2 = 1$$

In this equation, if p is assumed to be dominant, then p^2 is the frequency of homozygous dominant (AA) individuals in a population, 2pq is the frequency of

heterozygous (Aa) individuals, and q^2 is the frequency of homozygous recessive (aa) individuals.

From observations of phenotypes, it is usually only possible to know the frequency of homozygous dominant or recessive individuals, because both dominant and recessives will express the distinguishable traits. However, the Hardy-Weinberg equation allows us to determine the expected frequencies of all the genotypes, if only p or q is known. Knowing p and q, it is a simple matter to plug these values into the Hardy-Weinberg equation ($p^2 + 2pq + q^2 = 1$). This then provides the frequencies of all three genotypes for the selected trait within the population.

This illustration shows Hardy-Weinberg frequency distributions for the genotypes AA, Aa, and aa at all values for frequencies of the alleles, p and q. It should be noted that the proportion of heterozygotes increases as the values of p and q approach 0.5.

Linkage disequilibrium

Linkage is the tendency of genes or DNA sequences (e.g. SNPs) to be inherited together as a consequence of their physical proximity on a single chromosome. The closer together the markers are, the lower the probability that they will be separated during DNA crossing over, and hence the greater the probability that they will be inherited together. Suppose a mutational event introduces a "new" allele in the close proximity of a gene or an allele. The new allele will tend to be inherited together with the alleles present on the "ancestral," chromosome or haplotype. However, the resulting association, called linkage disequilibrium, will decline over time due to recombination. Linkage disequilibrium has been used to map disease genes. In general, both allele and haplotype frequencies differ among populations. Linkage disequilibrium is varied among the populations, being absent in some and highly significant in others.

Quantification of the relative risk of observable outcomes of a Pharmacogenetics Trial

Let PlaR be the placebo response rate (0% (PlaR (100%) and TntR be the treatment response rate (0% (TntR (100%) of a classical clinical trial. ObsRR is defined as the relative risk between TntR and PlaR:

$$\text{ObsRR} = \text{TntR} / \text{PlaR}.$$

Suppose that in the treatment group there is a polymorphism in relation to drug metabolism such as the treatment response rate is different for each genotypic subgroup of patients. Let q be the allele a frequency of a recessive biallelic locus (e.g. SNP) and $p = 1 - q$ the allele A frequency. Following Hardy-Weinberg

equilibrium, the relative frequency of homozygous and heterozygous patients are as follow:

$$AA: p^2 \qquad Aa: 2pq \qquad aa: q^2$$

with

$$(p^2 + 2pq + q^2) = 1.$$

Let's define AAR, AaR, aaR as respectively the response rates of the AA, Aa and aa patients. We have the following relationship:

$$TntR = AAR \cdot p^2 + AaR \cdot 2pq + aaR \cdot q^2.$$

Suppose that the aa genotypic group of patients has the lowest response rate, i.e. a response rate equal to the placebo response rate (which means that the polymorphism has no impact on natural disease evolution but only on drug action) and let's define ExpRR as the relative risk between AAR and aaR, as

$$ExpRR = AAR / aaR.$$

From the previous equations, we have the following relationships:

$$ObsRR (ExpRR (1/PlaR$$

$$TntR / PlaR = (AAR \cdot p^2 + AaR \cdot 2pq + aaR \cdot q^2) / PlaR$$

The maximum of the expected relative risk, max(ExpRR), corresponding to the case of heterozygous patients having the same response rate as the placebo rate, is such that:

$$ObsRR = ExpRR \cdot p^2 + 2pq + q^2 \quad \Leftrightarrow \quad ExpRR = (ObsRR - 2pq - q^2) / p^2$$

The minimum of the expected relative risk, min(ExpRR), corresponding to the case of heterozygous patients having the same response rate as the homozygous non-affected patients, is such that:

$$ObsRR = ExpRR \cdot (p^2 + 2pq) + q^2 \quad \Leftrightarrow \quad ExpRR = (ObsRR - q^2) / (p^2 + 2pq)$$

For example, if $q = 0.4$, $PlaR = 40\%$ and $ObsRR = 1.5$ (i.e. $TntR = 60\%$), then $1.6 (ExpRR (2.4$. This means that the best treatment response rate we can expect in a genotypic subgroup of patients in these conditions would be 95.6% instead of 60%.

This can also be expressed in terms of maximum potential gain between the observed difference in response rates ($TntR - PlaR$) without any pharmacogenetic hypothesis and the maximum expected difference in response rates ($(\max(ExpRR) \cdot PlaR - TntR)$ with a strong pharmacogenetic hypothesis:

$$(\max(ExpRR) \cdot PlaR - TntR) = [(ObsRR - 2pq - q^2) / p^2] \cdot PlaR - TntR$$

$$\Leftrightarrow (\max(ExpRR) \cdot PlaR - TntR) = [TntR - PlaR \cdot (2pq + q^2) - TntR \cdot p^2] / p^2$$

$$\Leftrightarrow (\max(ExpRR) \cdot PlaR - TntR) = [TntR \cdot (1 - p^2) - PlaR \cdot (2pq + q^2)] / p^2$$

$$\Leftrightarrow (\max(ExpRR) \cdot PlaR - TntR) = [(1 - p^2) / p^2] \cdot (TntR - PlaR)$$

that is for the previous example,

$$(95.6\% - 60\%) = [(1 - 0.62)/0.62] * (60\% - 40\%) = 35.6\%$$

Suppose that, instead of one SNP, we have p loci of SNPs for one gene. This means that we have $2p$ possible haplotypes for this gene and $(2p)(2p-1)/2$ possible genotypes. And with 2 genes with p_1 and p_2 SNP loci, we have $[(2p_1)(2p_1-1)/2] * [(2p_2)(2p_2-1)/2]$ possibilities; and so on. Examining haplotypes instead of combinations of SNPs is especially useful when there is linkage disequilibrium enough to reduce the number of combinations to test, but not complete since in this latest case one SNP would be sufficient. Yet the problem of frequency above still remains with haplotypes instead of SNPs since the frequency of a haplotype cannot be higher than the highest SNP frequency involved.

Statistical Methods to be used in Objective Analyses

The statistical significance of the differences between variance frequencies can be assessed by a Pearson chi-squared test of homogeneity of proportions with $n-1$ degrees of freedom. Then, in order to determine which variance(s) is(are) responsible for an eventual significance, we can consider each variance individually against the rest, up to n comparisons, each based on a 2×2 table. This should result in chi-squared tests that are individually valid, but taking the most significant of these tests is a form of multiple testing. A Bonferroni's adjustment for multiple testing will thus be made to the P-values, such as $p^* = 1 - (1-p)^n$.

The statistical significance of the difference between genotype frequencies associated to every variance can be assessed by a Pearson chi-squared test of homogeneity of proportions with 2 degrees of freedom, using the same Bonferroni's adjustment as above.

Testing for unequal haplotype frequencies between cases and controls can be considered in the same framework as testing for unequal variance frequencies since a single variance can be considered as a haplotype of a single locus. The relevant likelihood ratio test compares a model where two separate sets of haplotype frequencies apply to the cases and controls, to one where the entire sample is characterized by a single common set of haplotype frequencies. This can be performed by repeated use of a computer program (Terwilliger and Ott, 1994, Handbook of Human Linkage Analysis, Baltimore, John Hopkins University Press) to successively obtain the log-likelihood corresponding to the set of haplotype frequency estimates on the cases ($\ln L_{case}$), on the controls ($\ln L_{control}$), and on the overall ($\ln L_{combined}$). The test statistic $2((\ln L_{case}) + (\ln L_{control}) - (\ln L_{combined}))$ is then chi-squared with $r-1$ degrees of freedom (where r is the number of haplotypes).

To test for potentially confounding effects or effect-modifiers, such as sex, age, etc., logistic regression can be used with case-control status as the outcome variable, and genotypes and covariates (plus possible interactions) as predictor variables.

5

Example 6**Exemplary Pharmacogenetic Analysis Steps**

In accordance with the discussion of distribution frequencies for variances, alleles, and haplotypes, variance detection, and correlation of variances or
5 haplotypes with treatment response variability, the points below list major items which will typically be performed in an analysis of the pharmacogenetic determination of the effects of variances in the treatment of a disease and the selection/optimization of treatment.

- 10 1) List candidate gene/genes for a known genetic disease, and assign them to the respective metabolic pathways.
- 2) Determine their alleles, observed and expected frequencies, and their relative
15 distributions among various ethnic groups, gender, both in the control and in the study (case) groups.
- 3) Measure the relevant clinical/phenotypic (biochemical / physiological) variables of the disease.
- 20 4) If the causal variance/allele in the candidate gene is unknown, then determine linkage disequilibria among variances of the candidate gene(s).
- 5) Divide the regions of the candidate genes into regions of high linkage
25 disequilibrium and low disequilibrium.
- 6) Develop haplotypes among variances that show strong linkage disequilibrium using the computation methods.
- 7) Determine the presence of rare haplotypes experimentally. Confirm if the
30 computationally determined rare haplotypes agree with the experimentally determined haplotypes.
- 8) If there is a disagreement between the experimentally determined haplotypes and
35 the computationally derived haplotypes, drop the computationally derived rare haplotypes, construct cladograms from these haplotypes using the Templeton (1987) algorithm.

- 9) Note regions of high recombination. Divide regions of high recombination further to see patterns of linkage disequilibria.
- 10) Establish association between cladograms and clinical variables using the nested analysis of variance as presented by Templeton (1995), and assign causal variance to a specific haplotype.
- 11) For variances in the regions of high recombination, use permutation tests for establishing associations between variances and the phenotypic variables.
- 12) If two or more genes are found to affect a clinical variable determine the relative contribution of each of the genes or variances in relation to the clinical variable, using step-wise regression or discriminant function or principal component analysis.
- 13) Determine the relative magnitudes of the effects of any of the two variances on the clinical variable due to their genetic (additive, dominant or epistasis) interaction.
- 14) Using the frequency of an allele or haplotypes, as well as biochemical/clinical variables determined in the *in vitro* or *in vivo* studies, determine the effect of that gene or allele on the expression of the clinical variable, according to the measured genotype approach of Boerwinkle et al (Ann. Hum. Genet 1986).
- 15) Stratify ethnic/ clinical populations based on the presence or absence of a given allele or a haplotype.
- 16) Optimize drug dosages based on the frequency of alleles and haplotypes as well as their effects using the measured genotype approach as a guide.

Example 7

Exemplary Pharmacogenetic Analysis Steps - biological function analysis

In many cases when a gene which may affect drug action is found to exhibit variances in the gene, RNA, or protein sequence, it is preferable to perform biological experiments to determine the biological impact of the variances on the structure and function of the gene or its expressed product and on drug action. Such experiments may be performed *in vitro* or *in vivo* using methods known in the art.

The points below list major items which may typically be performed in an analysis of the effects of variances in the treatment of a disease and the selection/optimization of treatment using biological studies to determine the structure and function of variant forms of a gene or its expressed product..

- 1) List candidate gene/genes for a known genetic disease, and assign them to the respective metabolic pathways.
- 2) Identify variances in the gene sequence, the expressed mRNA sequence or expressed protein sequence.
- 3) Match the position of variances to regions of the gene, mRNA, or protein with known biological functions. For example, specific sequences in the promotor of a gene are known to be responsible for determining the level of expression of the gene; specific sequences in the mRNA are known to be involved in the processing of nuclear mRNA into cytoplasmic mRNA including splicing and polyadenylation; and certain sequences in proteins are known to direct the trafficking of proteins to specific locations within a cell and to constitute active sites of biological functions including the binding of proteins to other biological constituents or catalytic functions. Variances in sites such as these, and others known in the art, are candidates for biological effects on drug action.
- 4) Model the effect of the variance on mRNA or protein structure. Computational methods for predicting the structure of mRNA are known and can be used to assess whether a specific variance is likely to cause a substantial change in the structure of mRNA. Computational methods can also be used to predict the structure of peptide sequences enabling predictions to be made concerning the potential impact of the variance on protein function. Most useful are structures of proteins determined by X-ray diffraction, NMR or other methods known in the art which provide the atomic structure of the protein. Computational methods can be used to consider the effect of changing an amino acid within such a structure to determine whether such a change would disrupt the structure and/or function of the protein. Those skilled in the art will recognize that this analysis can be performed on crystal structures of the protein known to have a variance as well as homologous proteins expressed from different loci in the human genome, or homologous proteins from other species, or non-homologous but analogous proteins with similar functions from humans or other species.

5) Produce the gene, mRNA or protein in amounts sufficient to experimentally characterize the structure and function of the gene, mRNA or protein. It will be apparent to those skilled in the art that by comparing the activity of two genes or their products which differ by a single variance, the effect of the variance can be determined. Methods for producing genes or gene products which differ by one or more bases for the purpose of experimental analysis are known in the art.

6) Experimental methods known in the art can be used to determine whether a specific variance alters the transcription of a gene and translation into a gene product. This involves producing amounts of the gene by molecular cloning sufficient for in vitro or in vivo studies. Methods for producing genes and gene products are known in the art and include cloning of segments of genetic material in prokaryotes or eukaryotic hosts, run off transcription and cell-free translation assays that can be performed in cell free extracts, transfection of DNA into cultured cells, introduction of genes into live animals or embryos by direct injection or using vehicles for gene delivery including transfection mixtures or viral vectors.

7) Experimental methods known in the art can be used to determine whether a specific variance alters the ability of a gene to be transcribed into RNA. For example, run off transcription assays can be performed in vitro or expression can be characterized in transfected cells or transgenic animals.

8) Experimental methods known in the art can be used to determine whether a specific variance alters the processing, stability, or translation of RNA into protein. For example, reticulocyte lysate assays can be used to study the production of protein in cell free systems, transfection assays can be designed to study the production of protein in cultured cells, and the production of gene products can be measured in transgenic animals.

9) Experimental methods known in the art can be used to determine whether a specific variant alters the activity of an expressed protein product. For example, protein can be produced by reticulocyte lysate systems or by introducing the gene into prokaryotic organisms such as bacteria or lower eukaryotic organisms such as yeast or fungus), or by introducing the gene into cultured cells or transgenic animals. Protein produced in such systems can be extracted or purified and subjected to bioassays known to those in the art as measures of the action of that particular protein. Bioassays may involve, but are not limited to, binding, inhibition, or catalytic functions.

10) Those skilled in the art will recognize that it is sometimes preferred to perform the above experiments in the presence of a specific drug to determine whether the drug has differential effects on the activity being measured. Alternatively, studies may be performed in the presence of an analogue or metabolite of the drug.

11) Using methods described above, specific variances which alter the biological function of a gene or its gene product that could have an impact on drug action can be identified. Such variances are then studied in clinical trial populations to determine whether the presence or absence of a specific variance correlates with observed clinical outcomes such as efficacy or toxicity.

12) It will be further recognized that there may be more than one variance within a gene that is capable of altering the biological function of the gene or gene product. These variances may exhibit similar, synergistic effects, or may have opposite effects on gene function. In such cases, it is necessary to consider the haplotype of the gene, namely the combination of variances that are present within a single allele, to assess the composite function of the gene or gene product.

13) Perform clinical trials with stratification of patients based on presence or absence of a given variance, allele or haplotype of a gene. Establish associations between observed drug responses such as toxicity, efficacy, drug response, or dose toleration and the presence or absence of a specific variance, allele, or haplotype.

14) Optimize drug dosage or drug usage based on the presence of the variant.

Example 8

Stratification of patients by genotype in prospective clinical trials.

In a prospective clinical trial, patients will be stratified by genotype to determine whether the observed outcomes are different in patients having different genotypes. A critical issue is the design of such trials to assure that a sufficient number of patients are studied to observe genetic effects.

The number of patients required to achieve statistical significance in a conventional clinical trial is calculated from:

$$1.1 \quad N = 2(z_{\alpha} + z_{2\beta})^2 / (\delta/\sigma)^2 \text{ (two tailed test)}$$

From this equation it may be inferred that the size of a genetically defined subgroup N_i required to achieve statistical significance for an observed outcome associated with variance or haplotype "i" can be calculated as:

$$1.2 \quad N_i = 2(z_\alpha + z_{2\beta})^2 / (\delta_i / \sigma_i)^2$$

If P_i is the prevalence of the genotype "i" in the population, the total number of patients that need to be incorporated in a clinical trial N_g to identify a population with haplotype "i" of size N_i is given by:

$$1.3 \quad N_g = N_i / P_i$$

It should be noted that N_g describes the total number of patients that need to be genotyped in order to identify a subset of N_i patients with genotype "i".

If genotyping is used as means for statistical stratification of patients, N_g represents the number of patients that would need to be enrolled in a trial to achieve statistical significance for subgroup "i". If genotyping is used as a means for inclusion, it represents the number of patients that need to be screened to identify a population of N_i individuals for an appropriately powered clinical trial. Thus, N_g is a critical determinant of the scope of the clinical trial as well as N_i .

A clinical trial can also be designed to test associations for multiple genetic subgroups "j" defined by a single allele in which case:

$$1.4 \quad N_g = \max (N_{gi}) \text{ for } i=1 \dots j$$

If more than one subgroup is tested, but there is no overlap in the patients contained within the subgroups, these can be considered to be independent hypotheses and no multiple testing correction should be required. If consideration of more than one subgroup constitutes multiple testing, or if individual patients are included in multiple subgroups, then statistical corrections may be required in the values of z_α or $z_{2\beta}$ which would increase the number of patients required.

It should be emphasized that a clinical trial of this nature may not provide statistically significant data concerning associations with any genotype other than "i". The total number of patients that would be required in a clinical trial to test

more than one genetically defined subgroup would be determined by the maximum value of N_g for any single subgroup.

The power of pharmacogenomics to improve the efficiency of clinical trials arises from the fact it is possible to have $N_g < N$. The goal of pharmacogenomic analysis is to identify a genetically define subgroup in which the magnitude of the clinical response is greater and the variability in response is reduced. These observations correspond to an increase in the magnitude of the (mean) observed response δ or a decrease the degree of variability σ . Since the value of N_i calculated in equation 1.2 decreases non-linearly as the square of these changes, the total number of patients N_g can also decrease non-linearly, resulting in a clinical trial that requires fewer patients to achieve statistical significance. If δ_i and σ_i are not different than δ and σ , then N_g is greater than N as given by $N_g = N_i / P_i$. Values of δ_i and σ_i that give $N_g < N$ can be calculated:

$$1.5 \quad N_g < N \text{ if: } P_i > [(\delta/\sigma)^2]/[(\delta_i/\sigma_i)^2]$$

It is apparent from this analysis that N_g is not uniformly less than N , even with modest improvements in the values for δ_i and σ_i .

As with a conventional clinical trial, the incorporation of an appropriate control group in the study design is critical for achieving success. In the case of a prospective clinical trial, the control group commonly is selected on the basis of the same inclusion criteria as the treatment group, but is treated with placebo or a standard therapeutic regimen rather than the investigational drug. In the case of a study with subgroups that are defined by haplotype, the ideal control group for a treatment subgroup with hapotype "i" is a placebo-treated subgroup with haplotype "i". This is often a critical control, since haplotypes which may be associated with the response to treatment may also affect the natural course of the disease.

A critical issue in considering control groups is that σ for the control group placebo treated population with haplotype "i" may not be equivalent to that of the control population. If so, 1.5 may overestimate the benefits of any reduction in σ_i in the treatment response group if there is not also a reduction in σ_i in the control group.

If σ of the treatment and control groups are not equivalent, δ would be still calculated as the difference in the response of the two groups, but σ would be

different in the two groups with values of σ_0 or σ_1 respectively. In this case, the number of patients in the genetically defined subgroup N_i would be defined by:

$$2.1 \quad N_i = (\sigma Z_\alpha + \sigma_i Z_\beta)^2 / \delta^2$$

The total number of patients that would need to be enrolled in such a trial would be the maximum of

$$2.2 \quad N \text{ or } N/P_i$$

It will be apparent that such an analysis remains sensitive to increases in δ , but is less sensitive to changes in σ which are not also reflected in the control group.

Certain analysis may be performed by comparing individuals with one haplotype against the entire normal population. Such an analysis may be used to establish the selectivity of the response associated with a specific haplotype. For example, it may be desirable to establish that the response or toxicity observed in a specific subgroup is greater than that associated observed with the entire population. It may also be of interest to compare the response to treatment between two different subgroups. If σ differs between the groups, then the estimate of the number of patients that need to be enrolled in the trial must be calculated using equations 2.1 with N being the maximum of N_i/P_i for the different subgroups.

Another issue in controls is the relative size of the treatment and control groups. In a prospectively designed clinical trial which selectively incorporates patients with haplotype "i" the number of patients in the control and treatment group will be essentially equivalent. If the control group is different, or if haplotypes are used for stratification but not inclusion, statistical corrections may need to be made for having populations of different size.

Example 9

Stratification of patients by phenotype.

The identification of genetic associations in Phase II or retrospective studies can be performed by stratifying patients by phenotype and analyzing the distribution of genotypes/haplotypes in the separate populations. A particularly important aspect of this analysis is that any gene may have only a partial effect on the observed outcome, meaning that there will be an association value (A) corresponding to the

fraction of patients in a phenotypically-defined subgroup who exhibit that phenotype due to a specific genotype/phenotype.

It will be recognized to those skilled in the art that the fraction of individuals who exhibit a phenotype due to any specific allele will be less than 1 (i.e. $A < 1$).

5 This is true for several reasons. The observed phenotype may occur by random chance. The observed phenotype may be associated with environmental influences, or the observed phenotype may be due to different genetic effects in different individuals. Furthermore, the construction of haplotypes and analysis of recombination may not group all alleles with phenotypically-significant variances within a single haplotype or haplotype cluster. In this case, causative variances at a single locus may be associated with more than one haplotype or haplotype cluster and the association constant A for the locus would be $A = A_1 + A_2 + \dots + A_n < 1$. It is likely that many phenotypes will be associated with multiple alleles at a given locus, and it is particularly important that statistical methods be sufficiently robust to identify association with a locus even if A_i is reduced by the presence of several causative alleles.

Statistical methods can be used to identify genetic effects on an observed outcome in patient groups stratified by phenotype, eg the presence or absence of the observed response. One such method entails determining the allele frequencies in two populations of patients stratified by an observed clinical outcome, for example efficacy or toxicity and performing a maximum likelihood analysis for the association between a given gene and the observed phenotype based on the allele frequencies and a range of values for A (the association constant between a specific allele and the observed outcome used to stratify patients).

25 This analysis is performed by comparing the observed gene frequencies in a patient population with an observed outcome to gene frequencies in a table in which the predicted frequencies of different alleles of the gene assuming different values of the association constant A for that allele. This table of predicted gene frequencies can be constructed by those skilled in the art based on the frequency of any specific allele in the normal population, the predicted inheritance of the effect (e.g. dominant or recessive) and the fraction of a subgroup with a specific outcome who would have that allele based on the association constant A .

For example, if a specific outcome was only observed in the presence of a specific allele of a gene, the expected frequency would be 1. If a specific outcome was never observed in the presence of a specific allele of a gene, the expected frequency would be 0. If there was no association between the allele and the observed outcome, the frequency of that allele among individuals with an observed outcome would be the same as in the general population. A statistical analysis can

be performed to compare the observed allele frequencies with the predicted allele frequencies and determine the best fit or maximum likelihood of the association. For example, a chi square analysis will determine whether the observed outcome is statistically similar to predicted outcomes calculated for different modes of inheritance and different potential values of A. P values can then be calculated to determine the likelihood that any specific association is statistically significant. A curve can be calculated based on different values of A, and the maximal likelihood of an association determined from the peak of such a curve. Methods for chi square analysis are known to those in the art.

A multidimensional analysis can also be performed to determine whether an observed outcome is associated with more than one allele at a specific genetic locus. An example of this analysis considering the potential effects of two different alleles of a single gene is shown. It will be apparent to those skilled in the art that this analysis can be extended to n dimensions using computer programs.

This analysis can be used to determine the maximum likelihood that one or more alleles at a given locus are associated with a specific clinical outcome.

It will be apparent to those skilled in the art that critical issues in this analysis include the fidelity of the phenotypic association and identification of a control group. In particular, it may be useful to perform an identical analysis in patients receiving a placebo to eliminate other forms of bias which may contribute to statistical errors.

Example 10

Amyotrophic Lateral Sclerosis

I. Description of Amyotrophic Lateral Sclerosis

Amyotrophic Lateral Sclerosis (ALS) is a degenerative neurological disease that primarily involves the motor neuron system. The disease is characterized by muscular atrophy, progressive weakness, fasciculations, spasticity, dysarthria, dysphagia, and respiratory compromise. Sensory, cognitive, oculomotor, and autonomic functions are spared. There are approximately 30,000 individuals with ALS in the U.S. with an estimated annual cost of \$300 million dollars. The majority of cases are sporadic and of unknown etiology, however approximately 5%-10% of ALS cases are inherited as an autosomal dominant trait (familial ALS). Superoxide dismutase 1 (SOD1) gene mutations are responsible for about 20% of familial ALS cases.

II. Current therapies for ALS

There are no compounds that halt or prevent the progressive neurodegeneration of ALS. Riluzole (RILUTEK[®]), a benzothiazole derivative, is approved for treatment of ALS based on data that it slows disease progression and modestly increases survival time and ventilator-free time.. Riluzole's mechanism of action is not completely understood, however pharmacological properties include: 1) an inhibitory effect on glutamate release, 2) inactivation of voltage dependent sodium channels, 3) downmodulation of signalling via excitatory amino acid receptors, particularly glutamate receptors. Unfortunately riluzole, which was introduced in 1996, produces a benefit in only a fraction of patients, and the effect is modest. For example, despite the increase in longevity there is no consistent increase in muscular strength or pulmonary function. Thus patients do not experience significant relief from symptoms. Patients and care givers quickly understood these limitations, and consequently the use of the drug has been limited. A 1997 study, conducted during the first 8 months after commercialization of riluzole, found that only 37% of patients (17 of 46) eligible for riluzole were interested in trying the drug. The most common reason given for not wanting to try riluzole was insufficient benefit.

III. *Limitations of Current Therapies for ALS*

As noted above, despite therapy with riluzole, in most ALS patients the disease progresses to debilitating and ultimately life-threatening symptoms. However, since there are no therapeutic alternatives, riluzole is frequently administered despite the modest efficacy. This practice increases the cost of ALS care significantly. In addition to unimpressive efficacy, riluzole therapy has been associated with elevation of serum ALT levels. Thus patients on riluzole should be monitored bimonthly for elevated liver enzymes, at significant cost. Other side effects, which occur infrequently, include neutropenia, asthenia, nausea, dizziness, decreased lung function, diarrhea, abdominal pain, pneumonia, vomiting, vertigo, paresthesia, anorexia, and somnolence. Attending to these iatrogenic effects further increases the costs associated with riluzin therapy.

IV. *Potential Impact of Genotyping on Drug Development for ALS*

There is already a well established genetic cause of some familial ALS cases: mutation of the SOD-1 gene. It is likely that genetic factors play a role in the pathogenesis of sporadic ALS and non-SOD1 linked familial ALS. Strong candidate genes include, for example, other scavengers of superoxide, the entire glutamate signal transduction pathway, calcium channels and genes involved in the production and degradation of neurofilaments. Stratification of clinical trial patients

by allelic variation in these or other candidate genes may reveal differences in response rate, duration or quality of response, or adverse events that would be useful in the development of a compound. Provided in this invention are additional genetic pathways implicated in the disease process or response to candidate therapies.

5 Variation in these genes may account for the observed variability in treatment response. Exemplary variations in the candidate genes are provided in Tables 12-17 and 18-23. The Detailed Description above describes how one skilled in the art would identify a candidate gene or genes, identify sequence variances, stratify patients, design clinical trials, and obtain regulatory approval of a pharmacogenetic test for optimal responders to an ALS treatment. Gene pathways including most
10 preferably, but not limited to, those genes that are listed in the gene pathway Table 2, and pathway matrix Table 7 and discussed in Section V. below are candidates for the genetic analysis and product development strategies described above.

15 Advantages of Pharmacogenetic Clinical Development of Agents for ALS

In view of the limitations of present therapy, the advantages of an ALS clinical development program that includes genetic stratification of patients in the analysis of response to candidate therapeutic interventions are numerous. First, it may be possible to identify a subpopulation that responds to a treatment at a higher
20 rate than the whole ALS population. This would address the demonstrated disinclination of ALS patients to expose themselves to therapies of limited effectiveness. It might also allow regulatory approval of therapies that do not produce a sufficient response in the unstratified population to justify approval. Second, it may be possible to identify patients who respond to a treatment only at
25 higher doses than most patients require, or respond preferentially to an altered dosing route or schedule. Such customization of therapy to individual genetic and biochemical differences may allow a higher overall response rate to be achieved, without requiring totally empirical dose adjustment in each patient. Third, it may be possible to identify patients in whom side effects are likely to occur. Such patients
30 could be offered alternative treatments. It is also worth noting that the type of benefit afforded by drugs such as RILUTEK® - a slowing of deterioration - will likely be most useful if the drug is started very early, before large numbers of neurons are gone. However the long term prophylactic use of medicines in well, or nearly well, individuals entails a different cost-benefit analysis than in already sick
35 individuals. Identification of patients that respond well to early neuroprotective therapy may be aided by the analysis of genetic determinants of treatment response.

Additional uses of genetic stratification in clinical development have been described above.

As an example of a candidate gene with DNA sequence variances potentially relevant to drug efficacy, safety, or both consider the glutamate aspartate receptor NMDA 2C, a member of the glutamate pathway. Described in this application are novel NMDA 2C DNA sequence variances that the inventors have recognized may affect response to drugs. (Diseases in which the glutamate pathway is likely to play a role are summarized in Table 7) Six DNA sequence variances have been identified in the NMDA 2C gene, five of which alter the encoded amino acid sequence. Several of the amino acid variances are nonconservative, including phenylalanine-valine, glycine-arginine and arginine-serine (see Table 13 for details). Seven DNA sequence variances are described in the NMDA 2A receptor (Table 13). The effect of one or more of these genetic polymorphisms on efficacy or safety of an ALS treatment could be tested in a clinical trial. For example, the goal could be optimization of patient selection for glutamate channel antagonist therapy of ALS by determining whether an ALS patient has a NMDA 2A or 2C receptor genotype against which a glutamate antagonist is more effective or safer.

Similarly, for genes belonging to the other pathways relevant to treatment of ALS (see tables 2 and 7) and polymorphisms in those genes (tables 13 and 19) a strong argument can be made that said polymorphisms (or sets of polymorphisms, or haplotypes) may affect efficacy or safety of drugs active against ALS, including, but not limited to, drugs listed below in Table 25 and related compounds. The candidate genes include, but are not limited to, modulators of glutaminergic, serotonergic, GABAergic, melatonergic and opiate pathways, as well as calcium channels, cytokines, factors that mediate growth, differentiation and apoptosis, the coagulation cascade, second messenger systems, detoxification genes, particularly relating to superoxide, protein degradation and cytoskeleton genes.

V. Therapeutic Strategies for ALS

The etiology of most ALS cases is unknown but may involve autoimmune responses, for example to calcium channels, injury due to excessive excitotoxic stimulation (especially via aspartate, glutamate and GABA receptors), impaired clearance of free radicals, imbalance of neurofilament turnover or possibly viral mediated destruction of motor neurons (e.g. herpes virus). A number of drug development programs are aimed at these postulated pathophysiologic mechanisms. For example, there are candidate therapeutic agents that down modulate immune reactivity, block or dampen excitatory neurotransmitter signalling, alleviate free radical injury, and interfere with a hypothesized viral infection of motor neurons.

Beyond the specific mechanisms of action enumerated above, there are many compounds in development that are intended to halt, retard, or prevent neural cell degeneration, or promote neural cell regeneration. Many such compounds are in clinical development programs for multiple neurological diseases. For example, gabapentin is a compound with complex and incompletely understood pharmacology, but it shows anticonvulsant, antinociceptive, anxiolytic and neuroprotective activity in animal models. In ALS animal models gabapentin prevents neuronal death. One of its actions may be inhibition of glutamate synthesis by branched-chain amino acid aminotransferase (BCAA-t). Other compounds in development for ALS target proteins involved in growth control and differentiation, protein processing, intracellular second messenger cascades and cytoskeletal proteins (see 25 below for specific compounds and Table 1 for the candidate genes that may affect response to those compounds).

Below in Table 25 the therapies in development for ALS categorized by mechanism of action. The listed candidate therapeutic intervention response in patients with ALS may be affected by polymorphisms in genes as described above in the Detailed Description.

Example 11

Dementia

I. Description of Dementia

Dementia is a general term for mental deterioration. clinical state characterized by a significant loss of function in multiple cognitive domains, not due to an impaired level of confusion. Diagnosis of dementia requires 1) assessment of an individual's current level of cognitive function with the ability to compare to past intellectual function, and 2) documenting a decline in intellectual function by serial examinations over time. A comprehensive, reliable, and universally accepted clinical classification of the clinical and neuropathological characteristics of senile dementia has been described. However, definitive diagnosis is obtainable only with pathological findings upon autopsy. Based upon these diagnoses, there are an estimated 4 million Americans with Alzheimer's disease (AD) and 10 million Americans with dementia of all types.

Besides AD, there are categories of dementia that include vascular dementia, lewy body disease, frontal lobe dementia, mixed dementia, and post-traumatic dementia. A number of different diseases or conditions are characterized by or involve loss of cholinergic function and/or defects in neuronal remodeling repair and may result in clinical symptoms of dementia. Among these are diseases such as Alzheimer's disease (AD), Huntington's disease, Parkinson's disease, and

amyotrophic lateral sclerosis (ALS). Dementia can further be a complication of the following: depression, drug intoxication, metabolic disorders, normal pressure hydrocephalus, subdural hematomas, and cerebrovascular insufficiency.

II. *Current Therapies for Dementia*

Current therapies for the treatment of dementia include enhancement of cortical cholinergic function. In general, approaches to replacement of cholinergic function can be characterized as either: 1) therapies that compensate for existing damage; and 2) therapies that halt, retard, or prevent cerebral damage. Ideally, a therapy targeting both mechanisms could potentially reverse existing damage. There are two broad mechanisms to enhance cerebral cholinergic function; 1) to block metabolism of acetylcholine via an acetylcholinesterase inhibitor, or 2) agonists at muscarinic or nicotinic receptors.

Acetylcholinesterase inhibitors have recently been approved for the use in patients with mild to moderate Alzheimer's disease. These agents (donepezil, Tacrine) selectively inhibit the acetylcholinesterase enzyme and increases levels of cortical acetylcholine. In randomized controlled clinical trials, donepezil was shown to improve both cognitive performance and global functioning. The improvements are modest and may not be apparent until up to three months after commencement of treatment.

III. *Limitations of Current Therapies for Dementia*

Despite the introduction of pharmacologic agents for the treatment of dementia, the mainstay of therapeutic management continues to be education, and support for caregivers, and treatment of complications. This is in part because the available acetylcholinesterase inhibitor (donepezil) has limited efficacy and has undesirable side effects. Thus, the clinician is faced with the dilemma of limited therapeutic alternatives and weighing the benefits against the side effects.

Limitations of Acetylcholinesterase Therapy due to Low Efficacy

Acetylcholinesterase inhibitors have limited efficacy; only a fraction (modest improvement in 40-50%) of patients respond to therapy. The extent and progression of loss of cortical cholinergic neurons limit the therapeutic benefit of acetylcholinesterase inhibitors. Long-term benefit of inhibition of acetylcholinesterase activity is unproven. Further, there is no clinical evidence supporting the use of acetylcholinesterase inhibitors in the prevention of AD or in the treatment of more severe stages.

An additional efficacy concern of the acetylcholinesterase inhibitor is the latent period before demonstrable clinical benefit. In the same period there may be concurrent neurodegeneration. Thus, the clinician has limited therapeutic alternatives, the patient may have limited response to therapy, and the disease progresses. In many cases, medical management of dementia is reduced to treatment of complications or supportive care.

Limitation of Acetylcholinesterase Therapy due to Toxicity or Undesired Side Effects

Toxicities associated with the use of acetylcholinesterase inhibitors are 1) vagotonic effect on the myocardium resulting in bradycardia and complications of other myocardial syndromes, 2) gastrointestinal complications such as nausea, vomiting, diarrhea, 3) lowering of seizure threshold (since seizures can be a complication of AD, this side effect may be confused with the progression of the disease).

Other acetylcholinesterase inhibitors have been shown to have a severe hepatotoxic effect, those products have been removed from the market or clinical development programs.

IV. Impact of Genotyping on Drug Development for Dementia

As previously indicated, the pathways and genes emphasize the relationship with Alzheimer's disease. In connection with the development of Alzheimers, it had been found that the presence of the ApoE4 allele was associated with an earlier development of the disease than other alleles, and further was associated with a decreased response to present acetylcholinesterase inhibitors, such as tacrine. The $\epsilon 4$ allele of Apolipoprotein E (ApoE) is a well-established risk factor for late onset Alzheimer's disease. The work of Poirier (1995) and Farlow (1998) suggests there are significant interactions between sex, ApoE genotype, and therapeutic response (ADAS-Cog scores) to the acetylcholinesterase inhibitor tacrine, with the $\epsilon 4$ allele generally associated with poor response and the effect being more notable in women than in men. ApoE is only part of the brain lipid transport pathway, however, and the interaction of allelic variation at other components of this pathway with drug response can also contribute to variation in therapeutic responses.

Sequence variance in the butyrylcholinesterase (BCHE) gene has been found to correlate with the development of Alzheimer's disease, as well as with treatment efficacy of both cholinomimetic and non-cholinomimetic drug therapies. In this case, the presence of at least one BCHE-k allele is predictive of the development of

Alzheimer's disease and is negatively correlated with treatment efficacy of tacrine (a cholinesterase inhibitor) and an experimental vasopressinergic drug (a non-cholinomimetic drug). The BCHE-k allele has a point mutation at nucleotide 1828 (a G to A substitution) which results in an ala539thr change. This polymorphism can
5 be readily detected by PCR amplifying a region surrounding the variance site and sequencing the amplification product to determine the nucleotide at the particular site.

A group of patients was treated with an experimental vasopressinergic drug (n = 91) and compared to patients administered a placebo (n = 108) without
10 segregation or stratification by BCHE or other allelic status. As evaluated using the Mini Mental State Examination (MMSE) over a twelve-week treatment period, no statistically significant improvement was shown for the treatment group. However, when the treatment group was stratified according to the presence or absence of a BCHE-k allele, those patients without such an allele showed a statistically
15 significant improvement while those having at least one of the BCHE-k alleles did not. Thus, the analysis provides an example of a gene where a patient sub-population was identified where a treatment showed a positive response even though no such positive response was found for the overall patient population. Indeed, those patients not having a k-allele are approximately three times more likely to
20 respond to the vasopressinergic drug than are patients having at least one k-allele.

The response of Alzheimer's disease patients treated with the cholinomimetic drug, tacrine, was also determined. Similar to the above, the MMSE test was utilized as an indicator of a positive response. The positive response rate was approximately two-fold higher in those patients not having a k-
25 allele than in those patients having at least one k-allele.

In addition, it was found that the presence of either or both of a BCHE-k allele and an apoE-4 allele was positively correlated with the development of Alzheimer's disease. For example, in patients over 75 years of age, the odds ratio of a patient having a BCHE-k allele was 2.3, the odds ratio for having a apoE-4 allele
30 was 2.0, and the odds ratio for the joint occurrence of both alleles was 17.5. Thus, the BCHE-k allele is an example where the presence of a variant allele is negatively correlated with the efficacy of treatment with drugs from multiple drug categories, and which is further positively correlated with the development of a particular disease. Thus, the variance status of such a gene is useful both as a prognostic tool
35 for disease risk, as well as for identifying likely drug responders versus non-responders for drug development and/or treatment selection.

The evidence that a variance in a gene involved in a pathway that affects drug response in patients with dementia, indicates and supports the theory that there

is a likelihood that other genes have similar qualities to various degrees. As drug research and development proceeds to identify more lead candidate therapeutic interventions for dementia, there is possible utility in stratifying patients based upon their genotype for these yet to be correlated variances. Further, as described in the Detailed Description, methods for the identification of candidate genes and gene pathways, stratification, clinical trial design, and implementation of genotyping for appropriate medical management of a given disease is easily translated for dementia. As described below in section V. below there are likely gene pathways as are those that are outlined in the gene pathway Table 2 and matrix Table 7.

Advantages of Pharmacogenomic Clinical Development of Therapies for Dementia

The advantages of a clinical research and drug development program that includes the use of polymorphic genotyping for the stratification of patients for the appropriate selection of candidate therapeutic intervention includes 1) identification of patients that may respond earlier to therapy, 2) identification of the primary gene and relevant polymorphic variance that directly affects efficacy, safety, or both, 3) identification of pathophysiologic relevant variance or variances and potential therapies affecting those allelic genotypes or haplotypes, and 4) identification of allelic variances or haplotypes in genes that indirectly affects efficacy, safety or both.

Based upon these advantages, designing and performing a clinical trial, either prospective or retrospective, which includes a genotype stratification arm will incorporate analysis of clinical outcomes and genetic variation associated with those outcomes, and hypothesis testing of the statistically relevant correlation of the genotypic stratification and therapeutic benefits. If statistical relevance is detectable, these studies will be incorporated into regulatory filings. Ultimately, these clinical trial data will be considered during the approval for marketing process, as well as, incorporated into accepted medical management of dementia.

By identifying subsets of patients with mild to moderate dementia that respond earlier to drugs or agents or experience enhanced efficacy, optimal candidate therapeutic interventions may reduce the period of time prior to relief of cognitive impairments. Appropriate genotyping and correlation to dosing regimen would be beneficial to the patient, caregivers, medical personnel, and the patient's loved ones.

Optimization of cholinomimetic mediated therapy of dementia further demonstrates the utility of selection of a potential dementia patient that has a predisposing genotype in which selective cholinomimetic are more effective and or are more safe. In considering an optimization protocol, one could potentially

predetermine variance or variances within the muscarinic cholinergic receptor, nicotinic cholinergic receptor, modulatory mechanisms of cholinergic neurotransmission, or cholinergic receptor mediated intracellular mechanism of action that is preeminently responsible for drug response. By embarking on the previously described gene pathway approach, it is technically feasible to determine the relevant genes within such a targeted drug development program for dementia.

V. Description of Mechanism of Action Hypotheses for Future Drug Development for the Therapy of Dementia

Drug development programs for the identification of novel drug or candidate therapeutic interventions are aimed at the underlying pathophysiologic mechanisms of the disease leading to clinical signs and symptoms of dementia. Current hypotheses include, but are not limited to, therapeutic development in one of the following areas: 1) replacement of cholinergic function, 2) acetylcholine pathway: biosynthesis, secretion, degradation, reuptake, and receptor binding, 3) CNS lipid transport/membrane repair pathway and gene identification, 4) inflammatory mediators, e.g. prostaglandin, prostacylin, and thromboxane pathway, and 5) constituents of AD lesions and AD genes. These are described in detail below.

A. Therapeutic Approaches for Replacement of Cholinergic Function

Because dementia is apparently related to a loss of cholinergic function in the neocortex and forebrain arising from death or atrophy of basal forebrain cholinergic neurons, replacement of cholinergic function has been shown to have therapeutic benefit. In general, novel approaches for the replacement of cholinergic function can be characterized as either: 1) therapies that compensate for existing damage; and 2) therapies that halt, retard, or prevent cerebral damage.

B. Therapeutic approaches that compensate for existing damage

The therapeutic approaches that may compensate for existing damage include modulating cholinergic deficit, modulating other neurotransmitter deficits, modulating immune or inflammatory mechanisms of neural damage, and modulation of metabolism of specific neurotransmitters. Although these novel therapies are aimed at existing or damage yet to occur, the underlying course of the disease will remain.

Potential therapies for the compensation for cholinergic deficit are 1) increase presynaptic production of acetylcholine, 2) enhance release of acetylcholine, 3) stimulate choline reuptake, 4) selective muscarinic agonists, 5)

anticholinesterase inhibitors, 6) mixed action anticholinesterases and muscarinic receptor ligands, and 6) nicotinic receptor agonists.

Potential therapies for the compensation for modulating other neurotransmitters are 1) selective NMDA agonists, and 2) other disorders of neurotransmitter function.

Potential therapies for the compensation for modulating immune or inflammatory mechanisms of neural damage are 1) antiinflammatory agents that suppress inflammation and 2) inhibition of amyloid precursor protein (APP) degradation.

Potential therapies that compensate for monoamine metabolite deficits are agents that affect monoamine oxidase type B enzyme activity, therapy for behavioral symptoms of neurotransmitter function in dementia, and compensate for immune or inflammatory mechanisms involved in neural cell destruction.

C. Therapeutic approaches that halt, retard, or prevent cerebral damage

In general therapeutic approaches that halt, retard, or prevent cerebral neural damage are currently either growth factors or modulation of the deposition of aberrant pathological depositions of metabolic by-products. These approaches include promotion of the growth and regeneration of cholinergic neurons and generally include growth factors that act on neurons, neural precursors, or glial cells. Growth factors include but are not limited to nerve growth factor (NGF), brain-derived growth factor (BDGF), neurotrophins, and leukemia inhibitory factor (LIF).

Prevention of amyloid plaque deposition includes modulation of APP gene expression, prevention of the development of amyloidogenic peptide, inhibition of amyloid aggregation/secretion, and APP antagonists. Prevention of the formation of neurofibrillary tangles includes modulation of the phosphorylation of tau proteins.

D. CNS Lipid Transport/Membrane Repair Pathway and Gene Identification

Brain Apolipoproteins: The six apolipoproteins known to be expressed in the brain are listed below. They are present on the surface of three major types of lipoproteins, one class enriched in A-I, but also containing most of the D,E, and J protein in the brain; one class composed principally of E with minor amounts of A-I, A-IV, D, and J; and a third minor class containing the majority of A-IV. Variation in the structure or expression of these apolipoproteins can modulate lipid transport and brain remodeling.

Lipoprotein Receptors: Six brain receptors for lipoproteins have been identified in man. These include the low density lipoprotein receptor (LDL-R), the LDL receptor-related protein (LRP), the very low density lipoprotein receptor

(VLDL-R), and the class A macrophage scavenger receptor, all of which are also expressed outside the brain. Two new protein with LDL receptor-like domains have recently been identified in human brain: Apolipoprotein E receptor type 2, and the SorLA-1 receptor. Alterations in the structure or expression of those receptors can affect binding of ApoE alleles (ApoE2, for example, has reduced affinity for the LDL receptor), and more generally will modulate the biology of lipid transport.

Lipoprotein docking and lipid mobilization: Heparin sulfate proteoglyans (HSPG) are responsible for initial binding of ApoE-bearing lipoproteins to cells. Removal of HSPGs with heparinase blocks binding, even in the presence of receptor (LDL-R or LRP). Therefore variations in biosynthetic enzymes of the HSPG pathway will influence lipoprotein uptake. Lipid hydrolysis by cholesterol ester transfer protein (CETP) effects the transport of lipids from lipoproteins into cells.

Cholesterol Metabolism: Acyl CoA:cholesterol acyltransferase and HMG CoA reductase are responsible for the metabolism of cholesterol, therefore variations in the metabolic pathway of cholesterol will influence availability of cholesterol.

Hormonal control of lipoproteins and lipoprotein receptors: The expression of lipoproteins and their receptors is under hormonal control. Clinical studies of tacrine for Alzheimer's disease have also shown reduced incidence of AD in women taking estrogen supplements post menopausally. Therefore, variation in hormone levels, hormone receptors, or hormone receptor signaling pathways will modulate response to acetylcholinesterase inhibitors, e.g., by affecting lipid transport and cholinergic remodeling or by other means. Hormone receptors that bind their physiologic ligand within the cytoplasm then become activated and cross the nuclear membrane include but are not limited to growth hormone, prolactin, estrogen, retinoic acid receptor, thyrotropin releasing hormone. Associated transcriptional co-activators include but are not limited to SRC-1, SRC-2 (TIF-2), SRC-3 (p/CIP:AIB1), P/CAF, CBP, E6-AP, TRIP230, SMRT, SRA, and N-CoR.

E. Prostaglandin, Prostacyclin, and Thromboxane Pathway

Inflammatory mediators, and in particular the products of arachidonic acid metabolism, play a role in the development of AD neuropathology.

There are several lines of evidence supporting the role of inflammatory or immunological processes in the pathogenesis of Alzheimer's disease. First, neurodegeneration in AD is accompanied by manifestations of immune reaction including activation of the complement cascade, accumulation and activation of microglia and presence of inflammatory cytokines and acute phase reactants in tissue of AD brains. Second, epidemiological studies suggest that use of non-steroidal anti-inflammatory drugs (NSAIDs) delays the clinical expression of

Alzheimer's disease. The development of selective COX inhibitors has led to renewed interest in the therapeutic potential of NSAIDs in AD.

Arachidonic acid formation pathway genes include phospholipase A2, phospholipase C β 3, and diacylglycerol lipase. PGG2 formation pathway genes include cyclooxygenase I, cyclooxygenase II. PGH2 formation pathway genes include PGG2 reductase. PGH2 metabolizing enzymes include PGH2 reductase, PGD2 reductase, PGH-PGE isomerase, and thromboxane A2 synthase. Receptors include PGF1a receptor, PGD2 receptor, PGE2 receptor, PG12 receptor, and thromboxane A receptor. Exemplary variances for genes above are shown in Tables 13 and 19.

F. Constituents of Alzheimer's Disease Lesions and AD Genes

The relative contribution of different pathogenetic mechanisms to the development of AD in specific patients can affect the degree of cholinergic impairment and hence the response to acetylcholinesterase inhibitors.

There is clear evidence that different pathogenetic mechanisms affect the onset and rate of progression of AD. The possible effects of such are several lines of evidence supporting the role of inflammatory or immunological processes in the pathogenesis of Alzheimer's disease. First, neurodegeneration in AD is accompanied by manifestations of immune reaction including activation of the complement cascade, accumulation and activation of microglia and presence of inflammatory cytokines and acute phase reactants in tissue of AD brains. Second, epidemiological studies suggest that use of non-steroidal anti-inflammatory drugs (NSAIDs) delays the clinical expression of Alzheimer's disease. The development of selective COX inhibitors has led to renewed interest in the therapeutic potential of NSAIDs in AD. Pathway genes include Tau protein, amyloid precursor protein, presenilin 1, and presenilin 2.

In Tables 13 and 19, there are listings of candidate genes and specific single nucleotide polymorphisms that may be critical for the identification and stratification of a patient population diagnosed with dementia based upon genotype. Current pathways that may have involvement in the therapeutic benefit of dementia include, but are not limited to, glutaminergic, serotonergic, dopaminergic, adrenergic, cholinergic, histaminergic, purinergic, GABAergic, glycinergic, nitric oxide, peptide protein processing, opiates, cholecystokinin, corticotropin releasing factor, thyroid stimulating hormone, somatostatin, adrenocorticotrophic hormone, vasoactive intestinal peptide, calcium or potassium channels, prostaglandin, cytokines, estrogen, clot formation, hemostasis, oxygenstress, mitochondrial

maintenance, protein maturation and degradation, second messenger cascade, growth, differentiation and apoptosis, cytoskeleton, secretion, amyloid processing, and lipid transport or metabolism gene pathways that are listed in Tables 1-6, 12-17 and 18-23. One skilled in the art would be able to identify these pathway specific gene or genes that may be involved in the manifestation of dementia, are likely candidate targets for novel therapeutic approaches, or are involved in mediating patient population differences in drug response to therapies for dementia.

A sample of therapies approved or in development for preventing or treating the progression of symptoms of dementia currently known in the art is shown in Table 27. In this table, the candidate therapeutics were sorted and listed by mechanism of action. Further, the product name, the pharmacologic mechanism of action, chemical name (if specified), and the indication is listed as well.

Based upon these varying approaches there are many products in development for dementia. In Table 27 below lists current therapies that are in development for U.S. marketing approval. Identification of genes in specific pathways and the link to specific agents or drugs may be useful to conduct clinical trials and achieve higher degrees of safety and efficacy. The listed candidate therapeutic interventions response in patients with dementia may be affected by polymorphisms in genes as described above.

Example 12

Depression

I. Description of Depression

Major depression is a psychiatric disorder distinguishable from normal grief, sadness, and disappointment as well as the dysphoria and demoralization often associated with medical illness. Depressive disorders are characterized by abnormally long term depressed mood and may be accompanied by delusions and hallucinations. Individuals suffering from depression have feelings of despair and intense sadness, exhibit mental slowing and loss of concentration, are preoccupied with pessimistic worry and inner self, and are agitated and tend toward self-deprecation. In some depressive disorders, mania is present usually in episodic intervals and in these cases depressed mood is replaced with feelings of grandiosity and may be accompanied by incoherent speech. Clinically, unipolar or bipolar depression are terms used to describe the two broad categories of depressive disorders characterized by the absence or presence of episodic mania, respectively.

II. Current Medical Management Strategies for Depression

Unipolar Depression

Depression is a wide-spread disease that requires improved therapeutic alternatives to the conventional agents that have been available since the 1960s. Current therapeutic candidates of unipolar or bipolar depression are as follows:

5 tricyclic antidepressants, tetracyclic antidepressants, lithium, monoamine oxidase (MAO) inhibitors, electroconvulsive therapy (ECT) and atypical agents such as PROZAC[®], WELLBUTRIN[®], and trazodone.

Bipolar Depression

10 Despite the difficulties of medical management of bipolar depression, advances have changed therapeutic outcomes. Therapies such as lithium, valproate, and carbamazepine, clozapine, and ECT have made a positive impact on the patient outcomes. Further, the importance of psychosocial issues for understanding patients illnesses and factors affecting treatment compliance are more fully realized.

15 For bipolar depression, mood stabilizers are the first line therapy and include: lithium, valproate, and carbamazepine. Adjunct therapies are used for the treatment of agitation, insomnia, or aggressive behaviors and include benzodiazepines and antipsychotics. ECT is useful as an alternative therapy in patients who are pregnant or are trying to conceive, unresponsive to standard therapy, unable to tolerate first line therapies, or are refractory to first line or adjunct therapies. ECT has been shown to be effective as stated above, as well as 54% effective in refractory patients.

20

There are additional therapies that have been used for the treatment of bipolar depression. For example, off-label use of clozapine, Ca⁺⁺ channel antagonists, gabapentin, and lamotrigine in diagnosed bipolar patients have been demonstrated to be effective at stabilizing mood. Gabapentin, has a higher safety profile during pregnancy, but has side effects of ataxia, fatigue and somnolence. Lamotrigine, by effectively lowering glutamine release is effective at stabilizing mood, but is associated with dizziness, headache, double vision, somnolence, headache, and rash. Other medications include valproate for euphoric mania, valproate for dysphoric mania or mixed mania, and clozapine with lithium or valproate for patients with rapid-cycling episodes.

25

30

III. Limitation of Current Therapies for Depression

35 Frequently, depression is undiagnosed and if detected, treatment often is inadequate. Therapy of depression is associated with undesirable side effects and/or simply fails to adequately manage the symptoms of the condition. Thus, there is a

need for ongoing improved development of antidepressant therapeutic alternatives to the currently available products.

Limitations of Current Therapies for Unipolar Depression

Although these agents or therapies are efficacious (e.g. 80% improvement following ECT; lithium effectively prevents relapses in 60% of patients) there are significant limitations to their use and are 1) the onset of action of antidepressant drugs is latent, 2) responsivity and efficacy is not uniform, 3) long-term treatment can lead to symptoms of drug resistance, 4) there is perceived inhibition of creativity and decreased energy, and 5) there are patients with refractory depression with no therapeutic alternatives.

Limitations of Current Therapies for Bipolar Depression

Bipolar depression patients have additional therapeutic concerns as compared to unipolar depression patients. For bipolar patients there is the added difficulty of treating depression episodes. The efficacy of antidepressants is not well founded or documented in bipolar depression. Further, antidepressants have been documented to induce manic or hypomanic symptoms. Therefore, mood stabilizers are the first line therapy with adjunct therapies during manic or depression episodes.

An additional therapeutic issue associated with bipolar patients is that many comorbid psychiatric disorders occur within the same patient not only hindering a diagnosis, but also therapy. For example, substance abuse disorders, panic disorders, obsessive-compulsive disorders, and impulsive control disorders are often present and potentially mask symptoms of bipolar depression.

IV. Impact of Pharmacogenomics on Drug Development for Depression

There are two genes that have been described having polymorphisms that affect antidepressant drug response, the serotonin transporter gene and the angiotensin converting enzyme that affects the metabolism of substance P. These two examples are described below.

The Serotonin Transporter Gene

The serotonin transporter gene (5-HTT) polymorphism provides an example of a recessive SNP polymorphism in the non-coding region with an impact on inefficacy of a 5-HTT selective drug.

The serotonin transporter (5-HTT) plays a critical role in the termination of the serotonin (5-HT) neurotransmission and represent the prime target for selective

serotonin reuptake inhibitors (SSRIs). A functional polymorphism in the transcriptional control region upstream of the 5-HTT coding sequence has been reported. It consists of a 44 –base pair insertion (long variant) or deletion (short variant). It has been demonstrated that the long (l) and short (s) variants of this 5-HTT gene-linked polymorphic region had different transcriptional efficiencies. *In vitro* studies showed that the difference in 5-HTT mRNA synthesis result in different 5-HTT expression and 5-HT cellular uptake (Lesch et al. Science 1996 274:1527-153). Recently, it has been shown that an SSRI (fluvoxamine) efficacy in delusional depression seems to be related to allelic variation within the promoter of the 5-HTT gene (Smeraldi et al. Mol. Psychiatry 1998; 3:508-511). Both homozygotes for the long variant (l/l) of the 5-HTT promoter and heterozygotes (l/s) showed a better response to fluvoxamine than homozygotes for the short variant (s/s). Interestingly, the addition of pindolol (a mixed adrenoreceptor and 5-HT1A antagonist) has been proposed as an augmentation therapy for non-responders or partial responders to SSRIs, and it appears that in the group treated with fluvoxamine plus pindolol all the genotypes acted like l/l treated with fluvoxamine alone. This supports the hypothesis that the effect of pindolol is related to its ability to block 5-HT1A autoreceptors, thus preventing a negative feed-back of 5-HT at somatodendritic level. Furthermore, the activation of 5-HT1A autoreceptors could modulate the clinical effect of the SSRIs-induced 5-HTT blockade.

The 5-HTT polymorphism represents an example of a gene allelic variance that affects the transcriptional control, and ultimately, the amount of available transporter protein. In these cases, the gene product concentration or protein availability affects the function of the native mechanism and ultimately the ability of the drug to intervene with physiological function. One skilled in the art, upon utilizing the techniques described in the detailed description, would be able to identify known variances within a candidate gene, provide a diagnostic test to identify individuals with that variance or variances, group the individuals based upon the identified genotype, and design and implement a clinical study to test the effect a candidate drug has on the the groups. In this example, the allelic differences may affect transcriptional or translational control of the 5-HTT gene. A skilled practitioner will be able to utilize the techniques known in the art to determine the effects of a variance or variances within a gene promoter region to be able to study the impact those allelic differences have on the safety or efficacy of SSRIs or any other candidate drugs affecting the 5-HT pathway. Further, this example underscores the ability of a skilled practitioner to be able to utilize methods known in the art to design a pharmacogenomics clinical trial when the allelic difference is within the gene promoter region.

The Angiotensin Converting Enzyme Gene and Substance P

The localization of substance P in brain regions that coordinate stress responses and receive convergent monoaminergic innervation suggested that substance P antagonists might have psychotherapeutic properties. Similar to clinically used antidepressant and anxiolytic drugs, substance P antagonists suppress isolation-induced vocalizations in guinea pigs. In a placebo-controlled trial in patients with moderate to severe major depression, robust antidepressant effects of the substance P antagonist MK-869 were consistently observed. In preclinical studies, substance P antagonists did not interact with monoamine systems in the manner seen with established antidepressant drugs. These findings suggest that substance P may play an important role in psychiatric disorders.

Substance P is highly metabolized by ACE (angiotensin converting enzyme) which is a good actual example of pharmacogenetics: It has a high allele frequency in normal individuals (D: 34%, I: 66%) and there are clinical studies clearly demonstrating its impact on ACE inhibitors.

Moreover, it has been shown that DD homozygous patients (11%) have a higher brain level of substance P than II homozygous patients (43%), with an intermediate level for heterozygous patients (46%).

Using results of the initial phase II trial, we expect that a substance P antagonist will have more impact on patients with high brain level of substance P (actually, the DD patients who are more at risk for affective disorders). As measure of response rate, starting with the standard measure of response defined as $\geq 50\%$ change from baseline to week 6 in total HAM-D21 score, 54% of the patients improved with MK-869 and 28% patients improved with placebo in the phase II trial.

In a recent clinical trial of MK-869 versus placebo, a similar response rate was observed for both groups (54% and 48% respectively). If the ACE variance is considered as a dominant SNP with regard to substance P metabolism, calculation of an unequivocal positive response rate in the DD subgroup (i.e., 100%) would require an equally similar response rate in the II subgroup, while assuming the DI subgroup response rate remains similar to placebo (i.e., 48%). In this case, MK-869 would be positive (100%) only in a fraction of the patients, e.g., one out of every five.

Approximately 25% of the responders should be DD homozygous; if not, the hypothesis is not valid. Then, if 25% are DD, the number of patients included in the failed trial should be enough to see a statistically significant difference between the DD subgroup and other patients, since we would need at least 56 patients to test for such a high relative risk ($100\% / 48\% = 2$).

This approach exemplifies the utility of high allele frequency polymorphisms. Further, when the treatment is not efficacious for all individuals (i.e. response rates vary between treatment groups is less than 15%) the allele frequency of a potentially interacting recessive SNP polymorphism should be relatively high (e.g. from 30% for a 15% difference in response rate to 60%). This corresponds to 16% or less of total patients (see example 18 and table below).

The evidence that a variance in a gene involved in a pathway affects antidepressive drug response, indicates and supports the idea that other genes have similar qualities to various degrees. As drug research and development proceeds to identify more lead candidate therapeutic interventions for depression, there is utility in stratifying patients based upon their genotype for these yet to be correlated variances. Further, as described in the Detailed Description, methods for the identification of candidate genes and gene pathways, stratification, clinical trial design, and implementation of genotyping for appropriate medical management of a given disease is easily utilized for depression. As described below in section V, below there are likely gene pathways such as those outlined in the gene pathway Table 2 and matrix Table 7.

Optimization of adrenergic control or ion channel modulation mediated therapy of epilepsy further demonstrates the utility of selection of a potential epilepsy patient that has a predisposing genotype in which selective adrenergic or agents are more effective and or are safer. In considering an optimization protocol, one can potentially predetermine variance or variances within the adrenergic receptor, ion channel or ion channel mediated mechanisms of neurotransmission, or adrenergic receptor mediated intracellular mechanism of action that is preeminently responsible for drug response. By embarking on the previously described gene pathway approach, it is technically feasible to determine the relevant genes within such a targeted drug development program for depression.

A sample of therapies in development for preventing or treating the progression of symptoms of depression currently known in the art is shown in table 28. In this table, the candidate therapeutics were sorted and listed by mechanism of action. Further, the product name, the pharmacologic mechanism of action, chemical name (if specified), and the indication is listed as well.

V. Mechanism of Action Hypotheses for Novel Therapies for Depression: Utility of Genotyping

Unipolar Depression

Unfortunately, to date the biological mechanism of major unipolar depression is unclear. However, studies of endocrine systems, neurotransmission, and neuroelectrophysiology have provided the basis for the generation of pathophysiologic hypotheses. These hypotheses have been supported by clinical data stemming from the success of conventional treatment of depression.

One such hypothesis is that there is pituitary-hypothalamic dysfunction in depressed patients. It has been observed that depressed patients commonly have elevated levels of cortical steroids in their urine and blood. Further, 50% of the patients with clinical depression will not secrete cortisol when subjected to the dexamethasone suppression test. Additionally, thyrotropin releasing hormone (TRH) stimulation of thyrotropin stimulating hormone (TSH) release is aberrant in depressed patients without an alteration of serum T3 or T4 concentrations and growth hormone, prolactin, gonadal hormones, corticotropin releasing factor (CRF), and melatonin have diminished physiologic responses.

Another hypothesis of the biological dysfunction of depression is that there is a neurotransmitter dysfunction due to a catecholamine-indolamine imbalance. This theory postulates that there is a required level of catecholamines and receptor sensitivity required for normal mood. In depression, there may be aberrant receptor insensitivity, depletion of amines, or a depletion of their synthesis or storage that leads to depression. Supporting this theory is that monoamine oxidase inhibitors increase the availability of catecholamines and indolamines and have been used clinically for the management of depression.

The cholinergic neurotransmitter system has been implicated in the manifestation of depression. It has been postulated that there is an imbalance of adrenergic and cholinergic control of neural transmission in patients with depression.

Electrophysiologic studies have shown that patients with depression have altered rapid eye movement (REM) sleep patterns, i.e. shortened REM latency, than non-depressed patients. Other studies have documented a correlation of the circadian rhythm and precipitation of depressive episodes during autumn and winter months and diminished ambient light during those times during the year.

In each of the theories posited and described above, satisfactory conclusions are limited. Conventional therapy of depression with tricyclic antidepressants has demonstrated that this treatment affects more than one neurotransmitter system due to either modification or alteration of the regulation of neurotransmitter receptors signaling pathways rather than acting solely at neurotransmitter receptor binding.

Novel therapies of unipolar depression include venlafaxine and mirtazapine. Both of these compounds show promise in clinical trials for the treatment of

depression. Venlafaxine is a mixed serotonergic and noradrenergic reuptake inhibitor. Mirtazapine has noradrenergic and serotonergic antidepressant mechanism of action. These two products have what looks to be superior action over tricyclic antidepressants or selective serotonergic inhibitors (SSRIs).

Bipolar Depression

Theories for the mechanism have been described. In one model, electrophysiological kindling and behavior sensitization underlie bipolar disorders and further increasing frequencies of episodes over time. In another model, there appears to be a desynchronization of circadian rhythm in bipolar patients.

As for depression, the catecholamine hypothesis presumes that mania is due to an excess of catecholamines and depression is due to their depletion. Noradrenergic and dopaminergic dysfunction have both been linked to depression. In both cases of dysfunction, there appears to be causal links, i.e. aberrant noradrenergic neurotransmission and L-dopa induced hypomania among bipolar patients, respectively. Amphetamines can produce hypomania in bipolar patients and dopaminergic antagonists are effective for severe mania.

The serotonergic hypothesis generalizes that low serotonergic transmission is responsible for mania and depression because low serotonergic inputs may result in defective neuromodulation. Other hypotheses include neurotransmitters, enzymes, neuropeptides, and theories involving endocrine and immunological systems. As in many other complex disorders of psychological function, these models fall short of adequately describing the disturbance. Future studies and drug development may provide insights to refined biological mechanism of bipolar depression.

In Tables 13, and 19, there are listings of candidate genes and specific single nucleotide polymorphisms that may be critical for the identification and stratification of a patient population diagnosed with depression based upon genotype. Current pathways that may have involvement in the therapeutic benefit of depression include glutaminergic, serotonergic, dopaminergic, adrenergic, cholinergic, purinergic, GABAergic, melatonin, peptide protein processing, opiates, oxytocin, neuropeptide Y, calcitonin/calcitonin gene related peptide, tachykinin, corticotropin releasing factor, vasopressin, calcium or potassium channels, prostaglandin, testosterone, oxygen stress, second messenger cascade, folate metabolism pathways that are listed in Tables 2, 7, 13, and 19. One skilled in the art would be able to identify these pathway specific gene or genes that may be involved in the manifestation of depression, are likely candidate targets for novel therapeutic approaches, or are involved in mediating patient population differences in drug response to therapies for depression.

In Table 28 below is a list of the available candidate therapeutic alternatives available or in development for depression. There are listed by therapeutic approach are defined and listed in Table 2. The listed candidate therapeutic interventions response in patients with depression may be affected by polymorphisms in genes as described above.

Example 13

Epilepsy

I. Description of Epilepsy

Epilepsy is a neurological disorder affecting an estimated 1.8 million Americans with estimated direct and indirect costs of illness to be approximately \$3 billion dollars. Epilepsy is characterized by the behavioral consequences of recurrent, spontaneous, transient paroxysms of abnormal brain activity. An epileptic attack or seizure may result in impaired consciousness, involuntary movements, autonomic disturbances, psychic or sensory disturbances. The fundamental etiology of epilepsy is thought to occur within the cerebral cortex or limbic cortex (hippocampus). Chronic epilepsy is the syndrome in which recurrent neuronal paroxysms that underlie ictal events are transient expression of more permanently physiological disordered cortex. In ascertaining the location and the diagnosis of epilepsy, one can determine patterns of uncoordinated cortex by examination of ictal and interictal EEG recordings. Interictal recordings of epilepsy patients have an appearance of brief discharges that can be recorded from the scalp. There is a noticeable spike-wave complex that is evident and is characterized by sharp negative transients followed by a slower wave. The EEG spike-wave complex reflects a summation of highly synchronized abnormal neuronal membrane potentials that upon inspection appear as large paroxysmal depolarization shifts followed by prolonged after depolarizations.

Epilepsy can be divided into the following categories based upon etiology: 1) primary epilepsy which is an intrinsic, nonprogressive, hereditary group of cerebral disturbances, 2) secondary epilepsy which is symptomatic of some known pathologic processes affecting the brain, and 3) reactive seizures which are characterized by natural reaction to physiologic stress or transient ischemic injury.

Epilepsy can be categorized into the following categories: partial seizures, generalized seizures, and seizures of unknown origin. Partial seizures are initiated (uni- or bilaterally) in discrete focal areas in the cortex and remain focal lesions. Generalized seizures begin either uni- or bilaterally and spread throughout the cortical tissue. In either case the mechanism of epileptogenic activity is to date unknown. However, there is evidence suggesting the etiology of epilepsy.

Partial seizures can be further subcategorized into: 1) simple partial seizure disorders, consciousness not impaired (with motor signs or symptoms, with somatosensory or special sensory symptoms (e.g. simple hallucinations, such as tingling, light flashes, buzzing), with autonomic signs and symptoms (e.g. epigastric sensation, pallor, sweating, flushing, piloerection and pupillary dilation), with psychic symptoms (e.g. disturbances of higher cerebral function (déjà vu, fear, distortion of time perception)); or 2) complex partial seizure disorders (simple partial onset following impairment of consciousness, impairment of consciousness at onset); or 3) partial seizures evolving to generalized tonic clonic seizures (simple partial seizures evolving to generalized seizures, complex partial seizures evolving to generalized seizures, and simple partial seizures evolving to complex partial seizures and further evolving to generalized seizures). A key feature of partial epilepsy is auras. These somatosensory or special sensory symptoms manifest as sensations described above and precede the seizure. There are cases whereby pharmacotherapy reduces the frequency and severity of partial seizures but may have little to no effect on aura sensation in partial epilepsy patients.

Generalized seizures are divided into 1) nonconvulsive seizures (absence seizures, atypical seizures, myoclonic seizures, or atonic seizures), or 2) convulsive seizures (tonic-clonic seizures, tonic seizures, or clonic seizures). Other seizure disorders that do not fit into the above categories are some cases of neonatal and infantile seizures.

There are other factors that one must consider when diagnosing seizure disorders. A generalized seizure may be the result sleep deprivation, alcohol or sedative drug withdrawal, use of convulsant drugs, fever, or acute head trauma. Furthermore, reversible toxic, infectious, or metabolic processes may induce recurrent generalized convulsions. Infantile febrile convulsions are an example of infancy and early childhood seizures that may or may not be indicative of a future epilepsy diagnosis.

Acquired epilepsy may be the result of congenital lesions, head trauma, infectious processes, brain tumors, cerebrovascular disease, systemic toxic and metabolic disturbances, hippocampal sclerosis, and miscellaneous disorders (collagen vascular disease, blood dyscrasias, cerebral gray matter degenerating diseases (allergic encephalopathy), presenile or senile dementias).

Epilepsy may be confused with clinical signs and symptoms of syncope, migraine, or pseudoseizures (nonepileptic psychogenic seizures). Usually, video/EEG monitoring of the patient during ictal and interictal periods allows trained personnel to distinguish epilepsy from these other clinical presentations.

II. *Current Medical Management of Epilepsy*

For the majority of patients, epileptic seizures can be controlled with antiepileptic drug therapy (in many cases, monotherapy) and may be withdrawn if the patient is seizure free for an extended period, usually 2 years. Some patients do not become free of seizures, despite therapy compliance. Persistent epilepsy, aside from deleterious effects on health, has psychosocial, behavioral, and cognitive consequences, which often impose financial burdens to patients, their loved ones, and society.

Based upon accurate diagnosis of the seizure type and seizure-associated physiology, appropriate therapy to reduce seizure frequency, severity, and epilepsy-associated behaviors can be identified. Diagnosis of epilepsy involves both identification of the epileptic syndrome and the type of seizure. Syndromes are identified based upon age of onset, EEG recording analysis, location of the epileptic region or site of epileptogenesis, type of seizure. The drugs available for medical management of epilepsy are divided by their use in the clinic; common forms of epilepsy are treated differently than partial or secondarily generalized tonic-clonic seizures disorders.

The current pharmacotherapy has three main mechanisms of action: 1) reduction of sustained repetitive firing of a neuron by promoting the inactivation state of voltage-activated Na⁺ channels; 2) enhanced GABAergic mediated presynaptic or postsynaptic inhibition of neural transmission; or 3) limiting the activation of specific voltage-activated Ca⁺⁺ channels (T current). Following these general mechanism of action, current anticonvulsant drugs act by 1) prolonging the inactivation of the Na⁺ channels thereby reducing the ability of neurons to fire at high frequencies, 2) affecting GABAergic neurotransmission by reducing the metabolism of GABA, acting at the GABA receptor, enhancing the Cl⁻ influx in response to GABA postsynaptically, or promoting presynaptic GABA release, or 3) reducing the flow Ca⁺⁺ T-type calcium channels reducing the pacemaker current that underlies the thalamic rhythm in spikes and waves in generalized absence seizures.

There are generally accepted first- and second-line drugs for each of the types of epilepsies and associated syndromes. For partial seizures they are carbamazepine and phenytoin (first-line) and gabapentin, lamotrigine, phenobarbital, primidone, tagabine, topiramate and valproic acid (second-line). For generalized seizures they are: absence seizures ethosuximide and valproic acid (first-line); lamotrigine (second-line); myoclonic seizures, valproic acid (first-line), acetazolamide, clonazepam, lamotrigine, or primidone (second-line)); tonic-clonic seizures valproic acid, carbamazepine, phenytoin (first-line), lamotrigine,

phenobarbital, primidone (second-line); absence epilepsy with onset in childhood
ethosuximide (first-line), valproic acid, lamotrigine (second-line); absence seizures
with onset in adolescence valproic acid (first-line), ethosuximide, lamotrigine
(second-line)); juvenile myoclonic epilepsy valproic acid (first-line), acetazolamide,
5 clonazepam, primidone, lamotrigine (second-line); infantile spasms (West's
syndrome corticotropin (first-line), clonazepam, valproic acid)); Lennox-Gastaut
syndrome valproic acid, lamotrigine (first-line), carbamazepine (second-line).

Because there is greater risk for refractory epilepsy in partial epilepsy
patients, there has been greater demand for the development of novel treatment
10 alternatives. Since 1993 and as stated above, the introduction of lamotrigine,
topiramate, tiagabine, and gabapentin have changed the medical management of
partial epilepsy. Although carbamazepine and phenytoin remain the mainstay
therapies, these additions to the antiepileptic arsenal have provided therapeutic
alternatives to this subset population of epilepsy patients.

15 In addition to AEDs, refractory epilepsy may benefit from surgical therapy to
remove the site of epileptogenesis or implantation of a device to stimulate the vagus
nerve. Surgical removal of cortical tissue can be successful therapy in up to two
thirds of certain selected epilepsy and can reduce the seizure frequency and severity
in others. However, surgical therapy of refractory epilepsy is underused, and is
20 often a delayed procedure. It has been estimated that there are approximately 50,000
epilepsy patients that could benefit from resective surgery, however, there are only
an estimated 1,500 surgeries performed each year. Potential reasons for the
profound difference in the potential number of surgical candidates and the number
of procedures include: limited number of surgical teams performing the resective
25 surgery; failure of primary physicians to identify potential candidates and to refer
them to surgical centers; reluctance of third party payers to provide coverage for the
costly presurgical diagnostic testing and procedures; and further, a reluctance on the
part of the patient to voluntarily elect removal of cortical tissue.

Vagal nerve stimulation for the treatment of some patients with epilepsy has
30 proven to be safe and well tolerated. A device is implanted in the upper quadrant
that can be programmed to directly stimulate the vagal nerve. Stimulation of this
autonomic nerve has lead to a documented 25% reduction of seizure frequency in
refractory patients. The device does not appear to have similar efficacy when
implanted in a partial epilepsy patient population. The use of the surgically
35 implanted device has recently only been approved in the U.S. (June, 1997) for
patients over 12 years of age with known refractory partial epilepsy. Transient
hoarseness is a frequent side-effect of this device as a result of over-stimulation of
the vagal nerve.

III. *Limitations of Current Therapies for Epilepsy*

The limitations of current medical management of epilepsy are 1) partial response to therapy or refractory epilepsy, 2) undesired side effects, 3) continuing medical management of refractory or partial response in epilepsy patients, and 4) noncompliance.

Partial Response to Therapy and Refractory Epilepsy as a Therapeutic Limitation

Approximately 80% of patients with epilepsy are medically managed with current pharmacotherapy. In the remaining 20%, epileptic seizure frequency and severity are refractory to currently available medications. Medical personnel are left with attempting combination therapy of available anti-convulsive therapy. Standard regimens of multiple anticonvulsant therapy are fraught with greater tendency towards unwanted side effects. Interestingly, 20% of the primary generalized epilepsy patients and 35% of partial epilepsy patients are refractory. A poor response to anti-epileptic therapy may be result of many different therapeutic or diagnostic causes. Since the focus of therapeutic management of refractory epilepsy is combination antiepileptic drug therapy, the balance of beneficial therapy and the patient's intolerance of the adverse effects of the AEDs must be appropriately monitored.

Undesired Side Effects or Toxicities as a Therapeutic Limitation

All of the anti-epilepsy agents or compounds have undesired side effects. For example, nausea, dizziness, diplopia, ataxia, sedation, impaired mentation, hyperactivity, folic acid deficiency, leukopenia, elevated serum alkaline phosphatase levels, pruritis, blood dyscrasias, hirsutism, gingival hyperplasia, coarsening features, weight gain, and alopecia have been described for various anticonvulsant therapies.

Individuals with epilepsy have an increased rate of mortality as compared to the general population. Mortality is associated with treatment and with seizures and may include one or more of the following: trauma, burns, and drowning, habitual seizures with cardiopulmonary disease, severe aspiration, food bolus, and sudden unexplained death. Sudden unexplained death in epilepsy patients (SUDEP) has been reported as high as 1 in 270 patients that are refractory to antiepilepsy drugs, and is a statistic that does not include suicides.

Additional concern of combination therapy besides increased propensity to experience undesirable side effects is the effect of metabolic rates and blood levels of the combinations. There is ample literature on the effect one antiepileptic agent

has on another, for example carbamazepine decreases the blood levels of clanzepam, ethosuximide, methsuximide, primidone, tiagabine, topiramate, and valproic acid while increasing phenobarbital blood levels. Clonazepam decreases the blood levels of carbamazepine while decreasing primidone blood levels.

Continuous Medical Management as a Therapeutic Limitation

Antiepileptic drug (AED) therapy of epilepsy requires continuous medical monitoring. Factors involving lifestyle may trigger seizures in a patient diagnosed with epilepsy who have seemingly medically managed disease. For example, emotional stress, sleep deprivation, menstrual cycle, flickering lights and other sensory stimuli, alcohol use or withdrawal, or comorbidities (i.e. infections) may exacerbate seizures.

Noncompliance as a Limitation of Current Therapies

Noncompliance or partial compliance is a major concern in both monotherapy or combination therapy. Many patients who are in what appears to be remission, tend to noncompliance of their prescribed therapy. Determining plasma levels of the drug or drugs can monitor compliance, but this places an added burden on the patient and family members. Noncompliance can result from additional factors: missed medication, failure to refill the medication, a complicated dosing regimen, problems with memory or vision, postictal confusion, denial of medical condition, fear of teratogenic effects of the drug or drugs during pregnancy, concerns about the effects (both short and long-term) of the medication, and inability to afford the medication.

Clearly, for some patients, refined therapeutic management of seizure frequency and severity would have benefits above and beyond the clinical setting. Without many therapeutic alternatives to refine combination antiepileptic agent regimens, epilepsy poses a continued impact on health-related quality of life for each patient.

IV. Impact of Pharmacogenomics on Drug Development for Epilepsy

Genetic mechanisms of epilepsy have recently been described. However, the clinical genetics of seizure disorders has been a relatively slowly progressing field. Molecular genetic approaches have been useful to identify genes or gene clusters involved in linkage analysis.

Genetic polymorphism analysis and effects of antiepileptic drug therapy was recently described for the cytochrome P450 2C9 and 2C19 genes and these variance differences on the metabolic rates of phenytoin. The polymorphisms considered in

this study were the arg144cys and the ile359leu of the CYP2C9 gene and the *1, *2, and *3 polymorphisms of CYP2C19. In this study of 134 Japanese patients, the mean maximal metabolic rates of phenytoin were 42% lower in individuals having the ile359leu genotype. From this analysis, the authors conclude that patients with the ile359leu genotype may not tolerate higher daily doses of phenytoin and may require genetic identification prior to implementation of medical strategies.

The evidence that a variance in a gene involved in a pathway that affects antiepilepsy drug response, indicates and supports the expectation that there is a likelihood that other genes have similar qualities to various degrees. As drug research and development proceeds to identify more lead candidate therapeutic interventions for epilepsy, there is possible utility in stratifying patients based upon their genotype for these yet to be correlated variances. Further, as described in the Detailed Description, methods for the identification of candidate genes and gene pathways, stratification, clinical trial design, and implementation of genotyping for appropriate medical management of a given disease is easily translated for epilepsy. As described below in section V. below there are likely gene pathways as are those that are outlined in the gene pathway Table 2 and in the gene pathway and indication matrix Table 7.

Optimization of GABAergic or ion channel modulation mediated therapy of epilepsy further demonstrates the utility of selection of a potential epilepsy patient that has a predisposing genotype in which selective AED or agents are more effective and or are safer. In considering an optimization protocol, one could potentially predetermine variance or variances within the GABAergic receptor, ion channel or ion channel mediated mechanisms of neurotransmission, or GABAergic receptor mediated intracellular mechanism of action that is preeminently responsible for drug response. By embarking on the previously described gene pathway approach, it is technically feasible to determine the relevant genes within such a targeted drug development program for epilepsy.

A sample of therapies approved or in development for preventing or treating the progression of symptoms of epilepsy currently known in the art is shown in table 29. In this table, the candidate therapeutics were sorted and listed by mechanism of action. Further, the product name, the pharmacologic mechanism of action, chemical name (if specified), and the indication is listed as well.

V. Mechanism of Action Hypotheses for Novel Therapies for Epilepsy: Utility of Genotyping

Further studies have demonstrated that there is a genetic component to epilepsy. These genetic factors may predispose by an individual to epilepsy by

inheriting one or more of the following 1) low threshold for aberrant seizure activity; 2) traits that underlie certain specific primary epilepsy disorders; and 3) a disease of the CNS in which there are associated structural disturbances that produce seizures. As described above there is an urgent need for the discovery and development of therapeutic alternatives for the medical management of epilepsy. Recent research and development programs have included the following exemplary hypothesis testing programs. In a first hypothesis, glutamate neurotransmitter pathway has been implicated in aberrant excitatory neurotransmission. Glutamate and aspartate are ligands for the N-methyl-D-aspartate receptors and ionophore receptors (AMPA and Glu 1-4). Research efforts have been dedicated to eliciting glutaminergic specific antagonists that may be productive inhibitors of aberrant excitatory neural signals or may be effective to attenuate neural modulatory mechanisms that are defective in epileptogenic tissue.

Another hypothesis includes the glycinergic pathway. Because glycine is an additional excitatory neurotransmitter, efforts to identify glycinergic specific ligands that may be of therapeutic benefit to prevent, reduce, or ablate seizure activity in cortical tissue. A third hypothesis is the histamine receptor ligands and tachykinin receptor ligands may be useful for neuromodulation of excitatory neurotransmission.

Further, there may be genes within pathways that are either involved in metabolism of neurotransmitters or are involved in metabolism of various drugs or compounds. In Tables 1-6, 12-17 and 18-23, there are listings of candidate genes and specific single nucleotide polymorphisms that may be critical for the identification and stratification of a patient population diagnosed with epilepsy based upon genotype. Current pathways that may have involvement in the therapeutic benefit of epilepsy include glutaminergic, serotonergic, dopaminergic, adrenergic, cholinergic, purinergic, GABAergic, glycinergic, taurine, oxytocin, vasopressin, calcium, potassium, or sodium channels, mitochondrial maintenance, protein maturation and degradation, and second messenger cascade gene pathways that are listed in Tables 1-6, 12-17, 18-23. One skilled in the art would be able to identify these pathway specific gene or genes that may be involved in the manifestation of epilepsy, are likely candidate targets for novel therapeutic approaches, or are involved in mediating patient population differences in drug response to therapies for epilepsy.

Based upon these varying hypotheses there are many products in development for epilepsy. Table 29 below lists current therapies that have not yet received U.S. marketing approval. The listed candidate therapeutic interventions

response in patients with epilepsy may be affected by polymorphisms in genes as described above.

Example 14

Migraine

I. Description of Migraine

Migraine is a neurological syndrome that has multiple, complex manifestations. Migraine with auras, unilateral throbbing, and associated nausea is the basic clinical symptomatic presentation. The premonitory phase may be up to 24 hours and may be associated with auras or alterations of mood, appetite, visual, sensory, or motor functions. Migraine headache is a unilateral throbbing that is associated with photophobia, hypacusis, polyuria, and diarrhea.

There are many clinical subtypes of migraine. Broadly, these subtypes can be distinguished by the presence or absence of auras. Migraines without auras are defined as the classic type. Migraines with auras can be further classified as 1) migraine with typical auras, 2) migraine with prolonged auras, 3) familial hemiplegic migraine, 4) basilar migraine, 5) migraine without headache, and 6) migraine with acute-onset aura. Additional migraine types include ophthalmologic migraine and retinal migraine.

II. Current therapies for Migraine

Migraine medical therapy depends on the acute or prophylactic nature of the therapy and whether the migraine is diagnosed as mild, moderate, or severe. Many patients will take a step approach to each separate migraine attack, starting with weakly acting agents and progressing to more potent drugs. For patients with severe migraine, therapy includes prophylactic management.

Therapy for Acute Migraine

Mild migraine is a headache that may be accompanied by nausea, is unilaterally throbbing, and can be treated by nonprescription analgesics. Patients infrequently consult a neurologist for care of mild migraines because the level of impairment imparted by the headache portion is not debilitating and is relatively short lived. Mild migraine is thus treated with aspirin, acetaminophen, ibuprofen, indomethacin, naproxen sulfate, and in some cases antiemetic drugs (diphenhydramine, prochlorperazine, promethazine, and metchlorpramide).

Moderate migraine is generally characterized by similar symptoms of mild migraine, however the frequency and or severity are increased. Patients with

moderate migraine are generally not relieved with non-narcotic analgesics, and require medications that combine aspirin or acetaminophen with a mild sedative or α and β adrenergic receptor mediated vasoconstriction.

Severe migraine is characterized by similar symptoms as mild and moderate migraine. However, the severity and frequency of headache is debilitating. Patients seek relief from the headache pain in the acute stage and frequently require prophylactic maintenance therapy. The drugs used for the therapy of acute migraine are members of the ergot alkaloid family or sumatriptan.

The ergot alkaloids are partial agonists and antagonists for a variety of receptor types; serotonergic, adrenergic, dopaminergic, muscarinic, and GABAergic. Synthetic products with similar chemical structures to ergotamine predominantly are agonists at the serotonin subtype 1D or 1B. Both of these two subtypes act by inhibiting adenylyl cyclase activity in cortical neurons. Ergotamine is also a vasoconstrictor; this activity is thought to occur through activation of the α 1 adrenergic receptor system. Ergotamine is metabolized by undefined pathways and metabolites are excreted primarily in the bile. The bioavailability of ergotamine is approximately 1% due the potent first pass effect after parenteral delivery of the drug and erratic absorption between individuals.

Sumatriptan is another drug used for the acute, severe migraine attacks. Sumatriptan is a serotonin 1B, 1D selective receptor agonist. Because these receptor subtypes are auto receptors, activation of 5HT1B and 5HT1D receptors can act by controlling the release of the serotonin and other neurotransmitter release. Sumatriptan may also be efficacious in the treatment of migraine because it may block proinflammatory receptors at the level of nerve terminal in the perivascular space.

Other drugs used as adjunct therapy for acute, severe migraine attacks are corticosteroids and opioid analgesics. Due to their addictive qualities, opioid or narcotic analgesics are limited to acute, infrequent attacks.

Prophylactic Therapy of Migraine

There are currently six classes of standard treatments for the prophylactic therapy of migraine. They are 1) tricyclic antidepressants (amitriptyline), 2) 5HT antagonists (methylsergide), 3) β adrenergic receptor antagonists (propranolol, timolol, atenolol, metoprolol, nadolol), 4) monoamine oxidase inhibitors (depranil), 5) calcium channel blockers (verapamil, flunarizine), and 6) anticonvulsants (divalproex sodium, chlorpromazine). The criteria for the selection of prophylactic therapy are 1) patient has 6 or more headaches each month, 2) symptomatic medications are contraindicated or ineffective, 3) medication is necessary more than

twice each week, and 4) there is an expressed need on the part of the patient to prevent infrequent attacks, e.g. hemiplegic migraine, those headaches producing profound disruption, or those associated with a risk of stroke. The ultimate choice of the prophylactic medication is based upon the measured effect on the type of migraine and the patient's willingness to withstand the associated side effects.

III. Limitations of Current Therapies for Migraine

The current therapy of migraine includes management of acute attacks of the mild, moderate and severe categories. Therapies of severe migraine further include prophylactic therapies. Regardless of the acute or prophylactic nature of the therapy, there are both efficacy and toxicity limitations in which migraine remains problematic for medical management.

Toxicity or Undesired side effects of Acute Migraine Therapy

Ergotamine and its derivatives are useful drugs for the management of acute severe migraine attacks, however there are side effects associated with administration of the drug. Ergotamine is an activator of the CNS emetic centers, and nausea and vomiting are a frequent side effect that can be confused with a manifestation of the migraine attack. Other undesirable side effects are weakness of the legs, muscle pains, numbness and tingling of toes, and transient tachy- or bradycardia.

A known side effect of sumatriptan is coronary vasospasm and it is thus contraindicated in patients with ischemic heart disease or Prinzmetal's angina.

Limitations of Prophylactic Migraine Therapy

Although prophylactic therapy for migraine can reduce the frequency and intensity of the migraine attack, there are patients that achieve dramatic improvement and there are those that achieve only a 50% reduction, indicating a limited efficacy and benefit for a significant population subgroup. In those patients, the severity and intensity must be significant to require daily prophylactic medication.

Of the six categories of prophylactic agents all have associated side effects that may or may not be tolerable to each individual patient. They are 1) tricyclic antidepressants: sedation, dry mouth, weight gain, tremor, cardiac arrhythmias, aggravation of angle-closure glaucoma, and difficulty in urinating; 2) 5HT antagonist: weight gain, muscle cramps, vasoconstriction, and retroperitoneal pleuroperitoneal and subendocardial fibrosis; 3) β adrenergic receptor antagonists: aggravation of asthma, bradycardia, hypotension, fatigue, depression, masking the

symptoms of diabetes mellitus; 4) monoamine oxidase inhibitors: orthostatic hypotension, insomnia, and nausea; 5) calcium channel blockers: are not frequently used, however are associated with constipation and orthostatic hypotension; and 6) anticonvulsants: nausea, fatigue, weight gain, alopecia, tremor, liver dysfunction, and neural tube defects in developing embryos.

The least desired effect of prolonged prophylactic therapy of migraine is the associated increased frequency of headaches. Headaches, not of the migraine type, can occur daily and are related to rebound withdrawal from frequent use of the acute antimigraine medication. Patients experiencing this type of headache pattern are said to have transformed migraine and often experience episodic migraine attacks superimposed on their daily headaches. Ergotamines are frequently associated with chronic daily headaches, as are the triptans. Unfortunately, patients experiencing daily headaches are less likely to respond to acute therapy or any other preventative medications. Withdrawal of other migraine medications further render the patient more susceptible to daily headaches. Therefore, it is beneficial to prevent transformed migraine and chronic daily headaches. Drugs known to be associated with transformed migraine are generally limited to occasional use in patients that have greater than two migraines each month. It is additionally recommended for patients that experience more frequent headaches requiring over-the-counter or prescription medications be put on a rotating schedule.

IV. Impact of Pharmacogenomics on Drug Development for Migraine

As described above, there is evidence to suggest that there are efficacy and safety different responses to drug therapy within the migraine patient population. Although not all of these responses may be attributable to genotypic differences, it is expected that if stratification based upon genotype were performed, a reasonable correlation between drug response and genotype may become obvious. As described below, there are gene pathways that are involved with current drug therapy and those that may be potentially involved in the future. As described in the Detailed Description, methods for the identification of candidate genes and gene pathways, stratification, clinical trial design, and implementation of genotyping for appropriate medical management of a given disease is easily translated for migraine and patients diagnosed with migraine. As described below in section V. below there are likely gene pathways as are those that are outlined in the gene pathway Table 2 and matrix Table 7.

Optimization of serotonergic, nonsteroidal antiinflammatory, or cerebral vasoconstrictor mediated mechanism of therapy of migraine further demonstrates the

utility of selection of a potential migraine patient that has a predisposing genotype in which selective antimigraine or agents may be more effective and or have an more desirable safety profile. In considering an optimization protocol, one could potentially predetermine variance or variances within the serotonergic receptor pathway, nonsteroidal aninflammatory pathway, or serotonergic receptor or nonsteroidal antiinflammatory mediated intracellular mechanism of action that is preeminently responsible for antimigraine drug response. By embarking on the previously described gene pathway approach, it is technically feasible to determine the relevant genes within such a targeted drug development program for migraine.

A sample of therapies approved or in development for preventing or treating the progression of migraine currently known in the art is shown in Table 31. In this table, the candidate therapeutics were sorted and listed by mechanism of action. Further, the product name, the pharmacologic mechanism of action, chemical name (if specified), and the indication is listed as well.

Pharmacogenomics studies for these drugs, as well as other agents, drugs, compounds or candidate therapeutic interventions, could be performed by identifying genes that are involved in the function of a drug including, but not limited to is absorption, distribution metabolism, or elimination, the interaction of the drug with its target as well as potential alternative targets, the response of the cell to the binding of a drug to a target, the metabolism (including synthesis, biodistribution or elimination) of natural compounds which may alter the activity of the drug by complementary, competitive or allosteric mechanisms that potentiate or limit the effect of the drug, and genes involved in the etiology of the disease that alter its response to a particular class of therapeutic agents. It will be recognized to those skilled in the art that this broadly includes proteins involved in pharmacokinetics as well as genes involved in pharmacodynamics. This also includes genes that encode proteins homologous to the proteins believed to carry out the above functions, which are also worth evaluation as they may carry out similar functions. Together the foregoing proteins constitute the candidate genes for affecting response of a patient to the therapeutic intervention. Using the methods described above, variances in these genes can be identified, and research and clinical studies can be performed to establish an association between a drug response or toxicity and specific variances.

V. Description of Mechanism of Action Hypotheses for Future Migraine Drug Development

The pathogenesis of migraine includes the following theories: vascular, depression of cortical electrical activity, serotonergic abnormalities, alteration of

neurotransmitter modulation, and modulation of neuroendocrine mechanisms. These are described briefly below.

The vascular theory of migraine posits that there is abnormal cerebral blood flow and it apparently plays a pivotal role in the clinical symptoms of migraine. Studies have shown that a decrease in cerebral blood flow during an aura and an increase in blood flow during headache occur in migraine patients. This theory is somewhat substantiated indirectly by the pharmacologic action of therapies for acute migraine and prophylaxis, as previously described.

There have been additional studies that point to a mechanism of spreading depression of cortical electrical activity and a concurrent alteration of blood flow. This theory suggests that focal reduction of electrical activity and concurrent increase in blood flow occurs focally and spreads across the hemisphere at a rate of 2-3 mm each minute. This spreading hypothesis has been refined to a description of migraine as an evolving process in the cerebral cortex that occurs secondarily to decreased cortical function, decreased cortical metabolism, and or vasoconstriction of cortical arterioles.

Many studies have addressed the effect of serotonergic mechanism of the pathogenesis of migraine. These studies used the following premises: 1) there have been reports of decreased concentrations of serotonin in platelets and plasma, 2) increased levels of serotonin and serotonergic metabolites in urine, 3) lastly, migraine may be precipitated by abnormal release of biogenic amines, a theory borne out of the fact that reserpine and fenfluramine can precipitate a migraine attack.

Other theories propose that alterations of neurotransmitter systems e.g. nitric oxide, glutamate, and opioid receptors may be part of the pathogenesis of migraine. Further, Some studies have included anatomical differences in the raphe system and within the cerebral vasculature as well as alterations of the autonomic nervous system.

Therapy of migraine is dependent on the appropriate diagnosis, as well as the type, frequency, and severity of the throbbing headache. Upon diagnosis, patient education to identify and avoid trigger factors is a critical first step in all patients.

Trigger factors may include but are not exclusive to alcohol (red wine), foods (chocolate, certain cheeses), irregular sleep patterns, and acute changes in stress levels. Triggers may also come from environmental factors, such as time-zone shifts, high altitudes, or barometric changes. In women, menstrual cycles may trigger a migraine attack. These trigger factors suggest that there are complicating factors to include in any pathophysiologic hypothesis of migraine, and that these hypotheses may include neuroendocrine, endocrine, and other metabolic factors.

Further, there may be genes within pathways that are either involved in metabolism of neurotransmitters or are involved in metabolism of various drugs or compounds. In Tables -6, 12-17 and 18-23, there are listings of candidate genes and specific single nucleotide polymorphisms that may be critical for the identification and stratification of a patient population diagnosed with epilepsy based upon genotype. Current pathways that may have involvement in the therapeutic benefit of migraine include glutaminergic, serotonergic, dopaminergic, adrenergic, cholinergic, GABAergic, nitric oxide, peptide hormone processing, opiates, tachykinin, bradykinin, corticotropin releasing hormone, calcitonin/calcitonin gene related peptide, calcium channel, hemostasis, and second messenger cascade gene pathways that are listed in Tables -6, 12-17 and 18-23. One skilled in the art would be able to identify these pathway specific gene or genes that may be involved in the manifestation of migraine, are likely candidate targets for novel therapeutic approaches, or are involved in mediating patient population differences in drug response to therapies for migraine.

Based upon these varying hypotheses as stated above, there are many products in development for migraine. Table 31 below lists current therapies that have not yet received U.S. marketing approval.

Example 15

Psychosis

Psychosis is a general term for major mental disorder characterized by loss of contact with reality, often manifested by disordered thought, delusions or hallucinations. Psychosis can be part of several distinct psychiatric diseases, including schizophrenia, manic-depressive disease, severe depression with psychotic features, organic psychotic disorders, as well as in alcohol or drug intoxication and acute idiopathic psychotic illnesses. The most common of these is schizophrenia. The antipsychotic drugs are also used to treat non-psychiatric conditions such as, for example, nausea and vomiting, movement disorders associated with neurodegenerative diseases such as Huntington's disease and Tourette's syndrome, pruritis and chronic hiccough. Example 11 focuses predominantly on schizophrenia, however similar analysis, in terms of the relevant pathways, genes, polymorphisms and analytical methods for establishing relationships between polymorphisms and drug responses, would obtain in all the other diseases treated with antipsychotic drugs. Criteria for the diagnosis of schizophrenia and other psychoses, as well as diagnostic criteria for the other disorders treated with antipsychotics, are well established. (Diagnostic and

Statistical Manual of Mental Disorders, 4th ed., American Psychiatric Association Press, Washington, D.C., 1994.)

II. Current Medical Management of Schizophrenia

5 Over 15 drugs are approved for treatment of psychosis in the US. They include the so-called conventional or typical antipsychotic drugs and the more recently introduced atypical antipsychotic drugs. The former class includes phenothiazines (e.g. chlorpromazine, the first antipsychotic to be widely used), thioxanthenes (e.g. thiothixene), butyrophenones (e.g. haloperidol, one of the most
10 useful conventional antipsychotics) and other heterocyclic compounds. The atypical antipsychotics include compounds such as clozaril (the first, and best studied member of the class), risperidone, olanzapine, quetiapine, ziprasidone and iloperidone. Some drugs, such as loxapine, have pharmacology intermediate between that of the typical and atypical drugs.

15 The typical antipsychotics are believed to act predominantly by antagonizing dopamine receptors, particularly D2-dopamine receptors. These medications can be effective in reducing the positive symptoms of schizophrenia (hallucinations, delusions) but are generally not effective at alleviating the negative symptoms (withdrawal, flat affect, anhedonia, lack of will), nor do they generally result in
20 improved cognitive function. In fact, negative symptoms and cognitive function may worsen on typical antipsychotics. Typical antipsychotics exhibit dose dependent efficacy, and the optimal dose for a given patient must be determined empirically by gradually increasing the dose until adequate control of symptoms is achieved (without unacceptable side effects – see below). A therapeutic dose is
25 usually reached within 2-3 weeks of initiating therapy.

The atypical antipsychotic drugs have replaced the typical agents as front line therapy for schizophrenia and other psychoses because they have a beneficial impact on the negative symptoms as well as the positive symptoms of schizophrenia, and because, based on recent research, they may also improve cognitive function.
30 The atypical drugs affect a number of neurotransmitter systems, with modulation of serotonergic neurotransmission – particularly 5HT_{2C} receptor antagonism, a prominent effect in addition to modulation of dopaminergic function.. The best studied of this class of drugs is clozapine, which binds dopamine receptors with low affinity, and also interacts with muscarinic, adrenergic, serotonergic, and
35 histaminergic receptors. The table below depicts the relative receptor affinity (0-5

on a scale of 5, where 5 indicates a high affinity interaction) of a conventional drug (haloperidol) and an atypical drug (clozapine).

Relative Receptor Affinities of Haloperidol and Clozapine

	Neurotransmitter Receptor Subtype							
	D1	D2	5HT _{2A}	5HT _{1A}	α 1	α 2	H1	M1
Haloperidol	+3	+4	+1	0	+2	0	0	0
Clozapine	+2	+2	+1	+3	+3	+3	+4	+5

The effectiveness of the atypical antipsychotic drugs has revealed the inadequacy of a simplistic dopamine excess hypothesis of schizophrenia. The clinical effects of the atypical antipsychotic drugs are likely to reflect the summation of a complex set of interactions with a variety of neurotransmitter receptors. Interpatient differences in the function, levels or anatomical distribution of these different receptors are likely to account for a substantial fraction of interpatient variation in response to atypical antipsychotic drugs. Further, the function, levels and anatomical distribution of receptors is largely under genetic control, as is the associated biosynthetic, catabolic, recycling and signal transduction machinery. An understanding of the specific genetic variants that have major effects on drug efficacy would allow a far more sophisticated selection of appropriate therapy and dose than is possible currently.

III. Limitations of Current Therapies

The chief limitations of antipsychotic medicines are (i) conventional and atypical neuroleptic agents do not reduce the signs and symptoms of schizophrenia in all patients (an estimated one third to one quarter of psychotic patients are resistant to therapy); (ii) a wide range of serious adverse effects. Further, it is impossible to predict the response of any given patient, particularly the mix of drug effects on positive symptoms, negative symptoms, cognitive deficits and side effects. As a result, selection of therapy is at present completely empirical. This approach is costly, as (i) multiple physician visits may be required before an optimal dose of an effective agent is attained; (ii) even after determining an effective drug regiment, the long term effects of therapy in specific patients generally remain unknown, particularly with respect to side effects; (iii) these problems result in low rates of compliance with therapy. Hence there is a need for tools that would allow the prospective identification of patients likely to be responsive to - and free from short or long term side effects from - a particular drug.

Efficacy Limitations

The dilemma confronting psychiatrists and other clinicians selecting therapy for psychotic patients has been described by Baldessarini in Goodman and Gilman's The Pharmacological Basis of Therapeutics (9th edition) as follows: "No one drug or combination of drugs has a selective effect on a particular symptom complex in groups of psychotic patients; although individual patients may appear to do better with one agent than another, this can be determined only by trial and error". Thus, a clinician selecting therapy for a newly diagnosed psychotic patient, generally selects a compound with which he is comfortable, based on past experience. If that agent is not effective, or is producing a side effect, then a second agent is selected, again, entirely based on the physicians clinical judgement, and so on. This approach to optimization of pharmacotherapy has both medical and economic drawbacks. From the medical point of view, it does not always result in the selection of optimal treatment, with the attendant drawbacks in patient compliance. From an economic viewpoint the number of physician visits required to reach an effective dose of an effective drug are greater than necessary, and some patients may require hospitalization during the period when various drug regimens are being tested. There are other costs of using less than optimal therapy: (i) a patient might experience an improvement in cognitive symptoms on an optimal drug that would allow performance of a regular job; suboptimal therapy, even while adequately controlling positive symptoms, might not be sufficient to enable job performance. (ii) An optimal drug would minimize side effects, and thereby reduce physician visits, while also resulting in greater compliance. (Noncompliance is likely to ultimately lead to more hospitalization.) Determination of an optimal dose of an antipsychotic is another challenging aspect of therapy with these agents. Baldessarini (Goodman and Gilman, 9th ed.) writes: "Optimal dosage of antipsychotic drugs requires individualization to determine doses that are effective, well-tolerated, and accepted by a patient. Careful observation of the patients changing response is the best guide to dosage." As with selection of an optimal agent, discussed above, the determination of an optimal dose presently requires multiple physician visits. Clearly some fraction of interpatient variation in optimal dose level is likely due to genetic, and consequent biochemical differences between patients. Such differences may involve drug metabolizing enzymes or proteins that mediate pharmacodynamic effects. A list of such proteins is provided in Tables 1-6. Many typical antipsychotic drugs are metabolised by cytochrome P450 enzymes, with consequent wide interpatient variation in pharmacokinetic parameters. Further, many antipsychotic drugs are converted to active metabolites which can have

therapeutic effects or side effects. The metabolism of the tricyclic atypical drugs (clozapine, olanzapine, and quetiapine) occurs via N+-oxidation, N-glucuronidation, and phases 1 and 2 metabolism with final glucuronidation before renal excretion. The non-tricyclic atypical antipsychotic drugs (e.g. risperidone, sertindole and ziprasidone) have diverse chemical structures and there is less data on their metabolism, but it appears to include diverse phase 1 biotransformation reactions. As a rule, conventional antipsychotics are mainly effective against positive symptoms (hallucinations, delusions, illusions), while not significantly ameliorating negative symptoms (withdrawal and flat affect). They are also associated with a high incidence of adverse effects, particularly extrapyramidal symptoms (EPS) and tardive dyskinesia. Atypical antipsychotics constitute a significant improvement, in that they are at least as effective as conventional drugs against positive symptoms, they show at least some effectiveness against negative symptoms and, according to recent studies, they may also produce improvement in the cognitive deficits associated with schizophrenia (e.g. attention, executive function, short and long term memory), while causing substantially fewer extrapyramidal symptoms.

Toxicity Limitations

Unfortunately, conventional anti-psychotic drugs are uniformly associated with undesirable dose-dependent side effects. These include (but are not limited to) extrapyramidal effects, electrocardiogram abnormalities, sedation, weight gain, cognitive deficits, sexual or reproductive dysfunction, blood dyscrasias (particularly agranulocytosis associated with clozapine), , neuroleptic malignant syndrome (parkinsonism with catatonia), jaundice, skin reactions, epithelial keratopathy and seizures. Skin reactions include urticaria and dermatitis and are usually associated with phenothiazines. Epithelial keratopathy and corneal opacities are associated with chlorpromazine therapy. In extreme cases these effects impair vision, but they tend to spontaneously disappear upon discontinuation of chlorpromazine.

The extrapyramidal side effects of conventional neuroleptics include dystonia (facial grimacing, torticollis, oculogyric crisis), akathisia (feeling of distress or discomfort leading to restlessness or constant movement), and parkinsonian syndrome (rigidity and tremor at rest, flat facial expression).

Tardive dyskinesia is a common side effect of long term usage of conventional neuroleptic drugs. Tardive dyskinesia is a syndrome of abnormal involuntary repetitive, painless movements. These movements vary in intensity over time, dependent on the level of arousal or emotional distress. Typically there are

quick choreiform (ticlike) movements of the face, eyelids (blinks or spasms), mouth (grimaces), tongue, extremities, or trunk. Increasing the dose of the conventional neuroleptic agent can reverse extrapyramidal effects short term, but at the cost of more severe dyskinesia long term. Not infrequently a clinician is compelled to
5 change medication for a patient with adequately controlled schizophrenia because of dose related tardive dyskinesia or other extrapyramidal side effects..

Another important side effect of many antipsychotic drugs is QT wave prolongation, which has recently resulted in the withdrawal of an atypical antipsychotic compound. Cardiac conduction abnormalities associated with
10 antipsychotic therapy have resulted in patient deaths, presumably as a consequence of ventricular tachycardias. The mechanism of the conduction abnormalities appears to involve drug binding to cardiac potassium channels and consequent interference with repolarization current. Sertindole, for example, is a new antipsychotic agent that binds with high affinity (3-14 nM, depending on conditions) to and antagonizes
15 HERG, a cardiac potassium channel. The degree of interpatient variation in these effects is not well characterized. Genes likely to account for these differences encode potassium channels (which may also have some role in the central actions of these compounds), sodium channels and the genes associated with inherited forms of long QT wave syndrome (QT1, QT2, QT3, QT4, QT5 and QT6).

20 Yet another important side effect of antipsychotic drugs is weight gain which can lead to obesity.

IV. Impact of Genotyping on Drug Development for Schizophrenia

Most traditional neuroleptics have a narrow therapeutic-to-toxic index, and thus, the novel antipsychotics are the result of a search to substantially widen the
25 distance between the dose that treats psychosis and the one that produces adverse effects. In vitro binding profiles have been created for the atypical antipsychotics that have been approved by the U.S. Food and Drug Administration (FDA)-clozapine, olanzapine, and risperidone and those that are under FDA review-quetiapine and sertindole. These profiles, which were compared with that of the
30 typical neuroleptic haloperidol, provide guidance for predicting the adverse effects produced by these drugs. Most conventional antipsychotics have central nervous system effects, particularly extrapyramidal symptoms (EPS) and tardive dyskinesia, sedation, and dulling of cognition. Other adverse effects of the typical antipsychotics include the neuroleptic malignant syndrome, orthostatic hypotension,
35 changes in liver function, anticholinergic and antiadrenergic side effects, sexual

dysfunction, and weight gain. The newer agents have a lower incidence of EPS and tardive dyskinesia, while weight gain and changes in blood pressure and liver function tests are adverse effects that have been associated with the use of the newer agents. The favorable side effect profile of these new antipsychotics is likely to
5 make patients more willing to continue treatment, and thus these agents represent a step forward in the treatment of patients with severe, chronic mental illness.

This paper reviews the current literature describing the metabolism of both multi-receptor clozapine analogue atypical antipsychotic drugs (clozapine, olanzapine, and quetiapine) and serotonin-dopamine antagonist atypical
10 antipsychotic drugs (risperidone, sertindole and ziprasidone), to highlight the significance of those data in the context of clinical practice. The former group of atypical antipsychotic drugs shares a similar tricyclic structural nucleus and are metabolized through three major categorical metabolic pathways--N+-oxidation, N-glucuronidation, and phases 1 and 2 biotransformation with final glucuronidation
15 before renal excretion.

There have been reports of polymorphisms in key genes that affect neuroleptic activity in schizophrenic patients. For example, within the dopamine D4 receptor subtype, there are known tandem repeats in exon 3. In a recent study, schizophrenic patients on maintenance doses of chlorpromazine were stratified into
20 two groups, one having 2 tandem base pair repeats and the other having 4 tandem base pair repeats. Thirty-four percent of group one patients and 62% of group two patients had a favorable response to chlorpromazine therapy during acute stage treatments. The presence of homogeneous four 48 base pair repeats in both alleles in exon 3 of the dopamine D4 receptor subtype thus appears to be associated with
25 beneficial chlorpromazine response.

Recently, a study of the serotonin receptor subtype 6, polymorphism (T267T vs. C267T) in a group of patients refractory to clozapine therapy was reported. In this study, it appeared that the T267T genotype patients were more likely to respond to continued therapy than those patients with C267T genotype patients.
30 A recent report documented a correlation of the serotonin 5HTC2 receptor subtype biallelic polymorphism and neuroleptic efficacy. A significant number of schizophrenic patients homozygous for the allele C2 who responded unsatisfactorily to antipsychotic medication as compared to control.

Three polymorphisms in the serotonergic receptors, i.e. 5HT2A (T102C);
35 5HT2C (cys23ser); and 5HT2A (his452tyr) have reports of positive or negative correlation with efficacy of antipsychotic therapies. This disparity in the literature

will, in the future, be further examined in schizophrenic patient populations and correlation may be discovered.

The evidence that a variance in a gene involved in a pathway that affects neuroleptic drug response, indicates and supports the theory that there is a likelihood that other genes have similar qualities to various degrees. As drug research and development proceeds to identify more lead candidate therapeutic interventions for schizophrenia, there is possible utility in stratifying patients based upon their genotype for these yet to be correlated variances. Further, as described in the Detailed Description, methods for the identification of candidate genes and gene pathways, stratification, clinical trial design, and implementation of genotyping for appropriate medical management of a given disease is easily translated for schizophrenia. As described below in section V. below there are likely gene pathways as are those that are outlined in the gene pathway Table 2 and matrix table 7.

Identification of pathophysiologic relevant variance or variances and potential therapies affecting those allelic genotypes or haplotypes will speed the drug development. There is a need for therapies that are targeted to the disease and symptom management with limited or no undesirable side effects. Identification of a specific variance or variances within genes involved in the pathophysiologic manifestation of schizophrenia and specific genetic polymorphisms of these critical genes may assist the development of novel neuroleptic agents and the identification of those patients that may best benefit from therapy of these candidate therapeutic alternatives.

By identifying allelic variances or haplotypes in genes that indirectly affects efficacy, safety or both one could target specific secondary drug or agent therapeutic actions that affect the overall therapeutic action of conventional, atypical, or novel neuroleptic action.

A sample of therapies approved or in development for preventing or treating the progression of symptoms of schizophrenia currently known in the art is shown in Table 35. In this table, the candidate therapeutics were sorted and listed by mechanism of action. Further, the product name, the pharmacologic mechanism of action, chemical name (if specified), and the indication is listed as well.

V. Mechanism of Action Hypotheses for Novel Therapies for Schizophrenia: Utility of Genotyping

The underlying etiology of schizophrenia is not established, however there is compelling evidence that modulation of several neurotransmitter systems has an impact on the disease. As discussed above, conventional anti-psychotic drugs, effective in the management of schizophrenia, are dopamine antagonists, specifically D2-receptor antagonists, which block dopaminergic neurotransmission in the forebrain. Additionally, drugs such as mescaline and amphetamines, which are known to stimulate dopaminergic pathways, have been shown to induce psychotic symptoms. Evidence of dysfunctional serotonergic neurotransmission in schizophrenia includes evidence of altered serotonin receptor density, altered serotonin metabolism, and the evidence that serotonin receptors appear to be important targets for the atypical neuroleptics.

Based on current knowledge, there are three hypotheses that underscore the utility of polymorphic genotype analysis within the schizophrenic population. In the first, it could be considered that endogenous dopamine levels and consequential dopaminergic tone varies among schizophrenic patients, affecting response to receptor antagonists. These genetic DNA variations may affect brain neurotransmitter modulation of dopaminergic transmission and dopaminergic receptor mediated intracellular mechanisms among schizophrenic patients. In the second hypothesis, genetic DNA variations may affect the level of expression and brain distribution of dopamine receptors, imparting a variation in drug response among schizophrenia patients. Further, consideration of other endogenous neurotransmitters, i.e. serotonin, levels and consequential endogenous neurotransmitter tone varies among schizophrenic patients, affecting response to neurotransmitter receptor ligands or neurotransmitter receptor mediated intracellular mechanisms.

Further, there may be genes within pathways that are either involved in metabolism of neurotransmitters or are involved in metabolism of various drugs or compounds. In Tables 1-6, 12-17, and 18-23, there are listings of candidate genes and specific single nucleotide polymorphisms that may be critical for the identification and stratification of a patient population diagnosed with epilepsy based upon genotype. Current pathways that may have involvement in the therapeutic benefit of schizophrenia include glutaminergic, serotonergic, dopaminergic, adrenergic, cholinergic, histaminergic, GABAergic, glycinergic, opiates, cholecystokinin, neurotensin, tachykinin, calcium channels, and second messenger cascade gene pathways that are listed in Tables 1-6, 12-17, and 18-23. One skilled in the art would be able to identify these pathway specific gene or genes that may be involved in the manifestation of schizophrenia, are likely candidate

targets for novel therapeutic approaches, or are involved in mediating patient population differences in drug response to therapies for schizophrenia.

Example 16

Effect of Pharmacokinetic parameters on Efficacy of Drugs and Candidate Therapeutic Interventions

The efficacy of a compound is determined by a combination of pharmacodynamic and pharmacokinetic effects. Both types of effect are under genetic control. In the present invention, the genetic determinants of efficacy are discussed in terms of variation in the genes that encode proteins responsible for absorption, distribution, metabolism, and excretion of compounds, i.e. pharmacokinetic parameters.

The pharmacokinetic parameters with potential effects on efficacy include absorption, distribution, metabolism, and excretion. These parameters affect efficacy broadly by controlling the availability of a compound at the site(s) of action. Interpatient variability in the availability of a compound can result in undertreatment or overtreatment, or in adverse reactions due to levels of a compound or its metabolite(s). Differences in the genes responsible for pharmacokinetic variation, therefore, can be a potential source of interpatient variability in drug response.

Impact of Stratification Based Upon Genotype in Drug Development for Drugs, Compounds, or Candidate Therapeutic Interventions that may Efficacy

Clozapine induced agranulocytosis has been associated in some reports with specific HLA haplotypes or with HSP70 variants. These reports suggest that a gene within the HLA region is associated with agranulocytosis in response to clozapine therapy. In a recent study, two ethnic groups were analyzed for genetic markers for agranulocytosis. Tumor necrosis factor microsatellites d3 and b4 were found in higher frequencies in patients that experience clozapine-induced agranulocytosis. These data, while they need to be confirmed by additional studies, are suggestive that tumor necrosis factor polymorphisms may also be associated with clozapine-induced agranulocytosis.

In this invention we provide additional genes and gene sequence variances that may account for variability in toxic responses. The Detailed Description above demonstrates how identification of a candidate gene or genes (e.g. gene pathways), genetic stratification, clinical trial design, and diagnostic genotyping can lead to improved medical management of a disease and/or approval of a drug, or broader use of an already approved drug. Gene pathways including, but not limited to, those that are outlined in the gene pathway, Tables 1-6, preferably Table 3, are useful in

identifying the sources of interpatient variation in efficacy as well as in the adverse events summarized in the column headings of Table 8. Discussed in detail below are exemplary candidate genes for the analysis of pharmacokinetic variability in clinical development, using the methods described above.

5 Advantages of Inclusion of Pharmacogenetic Stratification in Clinical Development of Agents: Impact on Efficacy

As an example of identification of the primary gene and relevant polymorphic variance that directly affects efficacy, safety, or both one could select an gene pathway as described in the Detailed Description, and determine the effect
10 of genetic polymorphism and therapy efficacy, safety, or both within that given pathway. For example, referring to Table 8, genes involved in absorption and distribution, phase I and phase II metabolism, and excretion the optimization of therapy of by an agent known to have an efficacious effect by determining whether the patient has a predisposing genotype in which the selected agents are more
15 effective and or are more safe. In considering an optimization protocol, one could potentially predetermine the genotypic profile of these genes involved in the manifestation of the adverse effect, or those genes preeminently responsible for drug response. By embarking on the previously described gene pathway approach, it is technical feasibility to determine the relevant genes within such a targeted drug
20 development program.

Example 17

Drug-Induced Toxicity: Blood Dyscrasias

I. Description of Blood Dyscrasias

25 Blood dyscrasias are a feature of over half of all drug-related deaths and include, but are not limited to, bone marrow aplasia, granulocytopenia, aplastic anemia, leukopenia, lymphoid hyperplasia, hemolytic anemia, and thrombocytopenia. All of these syndromes include pancytopenia to some degree.

Bone marrow aplasia- is defined as a profound loss of bone marrow
30 resulting in pancytopenia. Drugs known to cause bone marrow aplasia include, but are not limited to, chloramphenicol, gold salts, mephenytoin, penicillamine, phenylbutazone, and trimethadione. In general these drugs are not first line therapy due to the rare occurrence of marrow aplasia. Specific forms of aplasia include:

Granulocytopenia- is defined as a loss of polymorphonuclear neutrophils to a
35 count lower than 500. Granulocytopenia primarily predisposes the patient to bacterial and fungal infections. Drugs known to cause granulocytopenia include, but are not limited to, captopril, cephalosporins, choral hydrate, chlorpropamide,

penicillins, phenothiazines, phenylbutazone, phenytoin, procainamide, propranolol, and tolbutamide.

Aplastic anemia- is a disorder involving an inability of the hematologic cells to regenerate and thus there is a dramatic depletion of one or more of the following cell types: neutrophils, platelets, or reticulocytes. Drugs associated with producing aplastic anemia are: 1) agents or compounds that produce bone marrow depression, for example cytotoxic drugs used in cancer chemotherapy; 2) agents or compounds that frequently, but inevitably, produce marrow aplasia, for example benzene; 3) agents or compounds that are associated with aplastic anemia, for example chloramphenicol, antiprotozoals, and sulfonamides.

Aplastic anemia is almost always a result of damage to the hematopoietic stem cells. There are two possible routes for the destruction of these cells: 1) direct damage to the stem cell DNA, and 2) cell cycle dependant depletion of later stage progenitor cells. In the first case, drugs or agents bind to and randomly damage the genetic material. This type of aplasia is associated with both early aplasia (immediate or direct cytotoxicity) or later myelodysplasia and leukemia. In the latter case, mitotically and metabolically active progenitor cells are preferentially affected and progenitor cell depletion may lead to unregulated proliferation of spared stem cells.

Leukopenia- is defined when the circulating peripheral white cell count falls below $5-10 \times 10^9$ cells per liter. Circulating leukocytes consist of neutrophils, monocytes, basophils, eosinophils, and lymphocytes.

Neutropenia is defined when the peripheral neutrophil count falls below 2×10^9 cells per liter. There are a number of drugs families that can cause neutropenia including, but not exclusive to, antiarrhythmics (procainamide, propranolol, quinidine), antibiotics (chloramphenicol, penicillins, sulfonamides, trimethoprim-methoxazole, para-aminosalicylic acid, rifampin, vancomycin, isoniazid, nitrofurantoin), antimalarials (dapson, quinine, pyrimethamine), anticonvulsants (phenytoin, mephénytoin, trimethadione, ethosuximide, carbamazepine), hypoglycemic agents (tolbutamide, chlorpropamide), antihistamines (cimetidine, brompheniramine, tripeleminamine), antihypertensives (methyldopa, captopril), antiinflammatory agents (aminopyrine, phenylbutazone, gold salts, ibuprofen, indomethacin), diuretics (acetazolamide, hydrochlorothiazide, chlorthalidone), phenothiazines (chlorpromazine, promazine, prochlorperazine), antimetabolite immunosuppressive agents, cytotoxic agents (alkylating agents, antimetabolites, anthracyclines, vinca alkyls, cis-platinum, hydroxyurea, actinomycin D), and other agents (alpha and gamma interferon, allopurinol, ethanol, levamisole, penicillamine).

Lymphoid hyperplasia- is characterized by reactive changes within the T-cell regions of the lymph node that encroach on, and at times appear to efface, the germinal follicles. In these regions, the T-cells undergo progressive transformation to immunoblasts. These reactions are encountered particularly in response to drug-induced immunoreactivity. Drugs known to cause lymphoid hyperplasia are phenytoin, and mephenytoin.

Hemolytic anemia- is characterized by the premature destruction of red cells, accumulation of hemoglobin metabolic by-products, and a marked increase in erythropoiesis within the bone marrow. Drugs known to cause hemolytic anemia include, but are not excluded to, methyldopa, penicillin, sulfonamides, and vitamin E deficiency.

Thrombocytopenia- is characterized by a marked reduction in the number of circulating platelets to a level below 100,000/mm³. Drug-induced thrombocytopenia may result from decreased production of platelets or decreased platelet survival or both. Drugs known to cause thrombocytopenia include, but are not excluded to, ethanol, acetaminophen, acetazolamide, acetylsalicylic acid, 5-aminosalicylic acid, carbamazepine, chlorpheniramine, cimetidine, digitoxin, diltiazem, ethchlorvynol, gold salts, heparin, hydantoins, isoniazid, levodopa, meprobamate, methyldopa, penicillamine, phenylbutazone, procainamide, quinidine, quinine, ranitidine, Rauwolfia alkaloids, rifampin, sulfonamides, sulfonylureas, cytotoxic drugs, and thiazide diuretics.

II. Impact of Stratification Based Upon Genotype in Drug Development for Drugs, Compounds, or Candidate Therapeutic Interventions that may Induce Blood Dyscrasias

Clozapine induced agranulocytosis is associated with differing HLA types and HSP70 variants in patients for whom responded to clozapine therapy but developed agranulocytosis. This is suggestive that a gene within the MHC region is associated with the manifestation of agranulocytosis in response to clozapine therapy. In a recent study, two ethnic groups were analyzed for genetic markers for the agranulocytosis. Tumor necrosis factor microsatellites d3 and b4 were found in higher frequencies in patients that experience clozapine-induced agranulocytosis. These data are suggestive that there is an involvement of tumor necrosis factor constellation polymorphism and clozapine-induced agranulocytosis.

There is evidence to suggest that there are safety response differences to drug therapy in reference to development of blood dyscrasias which may be attributable to genotypic differences between individuals. There is provided in this invention examples of gene pathways that are implicated in the disease process or its therapy and those that potentially cause this variability. The Detailed Description above

demonstrates how identification of a candidate gene or genes and gene pathways, stratification, clinical trial design, and implementation of genotyping for appropriate medical management of a given disease can be used to identify the genetic cause of variations in clinical response to therapy, new diagnostic tests, new therapeutic approaches for treating this disorder, and new pharmaceutical products or formulations for therapy. Gene pathways including, but not limited to, those that are outlined in the gene pathway Tables 1-6, preferably Table 3, and pathway matrix Table 8 and discussed below are candidates for the genetic analysis and product development using the methods described above.

Advantages of Inclusion of Pharmacogenetic Stratification in Clinical Development of Agents that May Cause Blood Dyscrasias

As an example of identification of the primary gene and relevant polymorphic variance that directly affects efficacy, safety, or both one could select an gene pathway as described in the Detailed Description, and determine the effect of genetic polymorphism and therapy efficacy, safety, or both within that given pathway. For example, referring to Table 8, genes involved in drug transport, phase I and phase II metabolism, protection from reactive intermediate damage, and immune responsiveness the optimization of therapy of by an agent known to have a blood dyscrasia side effect by determining whether the patient has a predisposing genotype in which the selected agents are more effective and or are more safe. In considering an optimization protocol, one could potentially predetermine the genotypic profile of these genes involved in the manifestation of the adverse effect, or those genes preeminently responsible for drug response. By embarking on the previously described gene pathway approach, it is technical feasibility to determine the relevant genes within such a targeted drug development program.

Example 18

Drug-Induced Toxicity: Cutaneous Toxicity

Drug-induced cutaneous toxicity includes, but is not excluded to, eczematous: photodermatitis (phototoxic and photoallergic), exfoliative dermatitis; maculopapular eruption; papulosquamous reactions: psoriaform, lichus planus, or pityriasis rosea-like; vesiculobullous reactions; txic epidermal necrolysis; pustular-acneform reactions; urticaria and erythemas: urticaria, erythema multiforme; nodular lesions: erythema nodosum, vasculitis reaction; telangiectatic and LE reactions; pigmentary reaction; other cutaneous reactions: fixed drug reactions, alopecia, hypertrichosis, macules, papules, angioedema, morbilliform-maculopapular rash, toxic epidermal necrolysis, erythema multiforme, erythema nodosum, contact

dermatitis, vesicles, petechiae, exfoliative dermatitis, fixed drug eruptions, and severe skin rash (Stevens-Johnson syndrome).

Drugs known to be associated with cutaneous toxicities include, but are not exclusive of, antineoplastic agents, sulfonamides, hydantoins and others listed for each type of toxicity.

Urticaria and angioedema- is defined as the transient appearance of elevated, erythematous pruritic wheals (hives) or seriginous exanthem. The appearance of urticaria is perceived as ongoing immediate hypersensitivity reaction. Angioedema is defined as urticaria, but involving deeper dermal and subdermal sites. Urticaria and angioedema appear to result from dilation of local postcapillary venules. Degranulation of cutaneous mast cells may be involved.

Drugs associated with urticaria and angioedema include, but are not excluded to, antimicrobials include, but not exclusive of, 5-aminosalicylic acid, aminoglycosides, cephalosporins, ethambutol, isoniazid, metronidazole, miconazole, nalidixic acid, penicillins, quinine, rifampin, spectinomycin, sulfonamides, and other drugs: asparaginase, aspirin and other non-steroidal antiinflammatory agents, calcitonin, chloral hydrate, chlorambucil, cimetidine, cyclophosphamide, daunorubicin, ergotamine, ethchlorvynol, doxorubicin, ethosuximide, ethylenediamine, glucocorticoids, melphalan, penicillamine, phenothiazines, procainamide, procarbazine, quinidine, tartazine, thiazide diuretics, thiotepa.

Morbilloform-maculopapular rash- are rashes that result in eruptions or are morbilliform in nature.

Drugs associated with rashes include, but are not limited to, 5-aminosalicylic acid, cephalosporins, erythromycin, gentamicin, penicillins, streptomycin, sulfonamides, allopurinol, barbiturates, captopril, coumarin, gold salts, hydantoins, thiazide diuretics.

Toxic epidermal necrolysis and erythroderma and exfoliative dermatitis-

Cutaneous erythroderma, edema, scaling, and fissuring may occur in response to certain drugs. Drugs associated with these types of cutaneous reactions include, but are limited to, allopurinol, amikacin, captopril, carbamazepine, chloral hydrate, chlorambucil, chloroquine, chlorpromazine, cyclosporine, diltiazem, ethambutol, ethylenediamine, glutethimide, gold salts, griseofulvin, hydantoins, hydroxychloroquine, minoxidil, nifedipine, nonsteroid antiinflammatory agents, penicillin, phenobarbital, rifampin, spironolactone, sulfonamides, trimethadione, trimethoprim, tocainamide, tocainide, vancomycin, verpamil.

Erythema multiforme- is characterized by a hypersensitivity reaction in blood vessels of the dermis. The hypersensitivity is the result of immune complexes formed by small molecules interacting with proteinaceous components of the blood

vessels. In cases whereby the mucosal membranes of the mouth and eye are involved, is referred to as Stevens-Johnson syndrome. Typically the cutaneous lesions, blisters and painful erosions occur in the mouth and eye.

Drugs associated with erythema multiforme include, but are not limited to, allopurinol, acetaminophen, amikacin, barbiturates, carbamazepine, chloroquine, chlorpromazine, clindamycin, ethambutol, ethosuximide, gold salts, glucocorticoids, hydantoins, hydralazine, hydroxyurea, mechlorethamine, meclofenamate, penicillins, phenothiazides, phenolphthalein, phenylbutazone, rifampin, streptomycin, sulfonamides, sulfonyleureas, sulindac, vaccines.

Fixed drug eruptions-

Drugs associated with fixed drug eruptions include, but are not excluded to, acetaminophen, 5-aminosalicylic acid, aspirin, barbiturates, benzodiazepines, barbiturates, chloroquine, dapsone, dimethylhydrazine, gold salts, hydralazine, hyoscine, ibuprofen, iodides, meprobamate, methamphetamine, metronidazole, penicillins, phenobarbital, phenolphthalein, phenothiazides, phenylbutazone, procarbazine, pseudoephedrine, quinine, saccharin, streptomycin, sulfonamides, and tetracyclines.

Erythema nodosum- is an inflammatory reaction in subcutaneous fat which represents a hypersensitivity reaction to a number of antigenic stimuli. Multiple red, painful nodules do not ulcerate but involute and leave a yellow-purple bruise. Small molecules interacting with proteinaceous components form a sensitizing antigen.

Drugs associated with producing erythema nodosum include, but are not excluded to, bromides, oral contraceptives, penicillins, and sulfonamides.

Contact dermatitis- is characterized by eruptions on histological analysis to epidermal intercellular edema (spongiosis). Contact dermatitis can be caused by allergic or irritant mechanisms. Allergic contact dermatitis is a delayed hypersensitivity reaction that can occur in response to a variety of small molecules that when bound to proteinaceous components of the skin form a sensitizing antigen. The antigen is processed by Langerhans' cells in the epidermis, presenting the antigen to the circulating T lymphocytes. Irritant dermatitis is produced by substances that irritate or have a direct toxic effect on the skin.

Drugs associated with contact dermatitis side effects include, but are not limited to, ambroxol, amikacin, antihistamines, bacitracin, benzalkonium chloride, benzocaine, benzyl chloride, cetl alcohol, chloramphenicol, chlorpromazine, clioquinol, colophony, ethylenediamine, fluorouracil, formaldehyde, gentamycin, glucocorticoids, glutaraldehyde, heparin, hexachlorophene, iodochlorhydroxyquin, lanolin, local anesthetics, minoxidil, naftin, neimycin, nitrofurazone, opiates, para-

aminobenzoic acid, parabens, penicillins, phenothiazines, proflavine, propylene glycol, streptomycin, sulfonamides, thimerosal, timolol.

5 *Impact of Stratification Based Upon Genotype in Drug Development for Drugs, Compounds, or Candidate Therapeutic Interventions that May Induce Cutaneous Reactions*

10 Recently, it has been described that there is a deletion polymorphism in the B2 bradykinin receptor gene (B2BKR). It was revealed that there is a 9 base pair deletion in exon 1 of the B2BKR gene and upon inspection of patients experiencing angioedema, patients with immunochemical evidence of angioedema were homozygous for no deletion at that site. These results were suggestive of B2BKR genotype influence on the clinical status and manifestation angioedema.

15 There is evidence to suggest that there are safety response differences to drug therapy in reference to development of cutaneous reactions which may be attributable to genotypic differences between individuals. There is provided in this invention examples of gene pathways that are implicated in the disease process or its therapy and those that potentially cause this variability. The Detailed Description above demonstrates how identification of a candidate gene or genes and gene pathways, stratification, clinical trial design, and implementation of genotyping for appropriate medical management of a given disease can be used to identify the genetic cause of variations in clinical response to therapy, new diagnostic tests, new therapeutic approaches for treating this disorder, and new pharmaceutical products or formulations for therapy. Gene pathways including, but not limited to, those that are outlined in the gene pathway Tables 1-6, more preferably Table 3, and pathway matrix Table 8 and discussed below are candidates for the genetic analysis and product development using the methods described above.

20 Advantages of Inclusion of Pharmacogenetic Stratification in Clinical Development of Agents that May Cause Cutaneous Reactions

30 As an example of identification of the primary gene and relevant polymorphic variance that directly affects efficacy, safety, or both one could select an gene pathway as described in the Detailed Description, and determine the effect of genetic polymorphism and therapy efficacy, safety, or both within that given pathway. For example, referring to Table 8, genes involved in drug transport, phase I and phase II metabolism, protection from reactive intermediate damage, and immune responsiveness, the optimization of therapy of by an agent known to have a cutaneous side effect by determining whether the patient has a predisposing

35

genotype in which the selected agents are more effective and or are more safe. In considering an optimization protocol, one could potentially predetermine the genotypic profile of these genes involved in the manifestation of the adverse effect, or those genes preeminently responsible for drug response. By embarking on the previously described gene pathway approach, it is technical feasibility to determine the relevant genes within such a targeted drug development program.

Example 19

Drug-Induced CNS Toxicity

Drug-induced central nervous system toxicity includes CNS stimulation or CNS depression. Characteristics of CNS toxicity include, but are not limited to, tinnitus and dizziness, acute dystonic reactions, parkinsonian syndrome, coma, convulsions, depression and psychosis, sweating, mydriasis, hyperpyrexia, centrally mediated cardiovascular involvement (hypertension, tachycardia, extrasystoles, arrhythmias, circulatory collapse) and respiratory depression or tachypnea. Drugs known to be associated with CNS toxicity include, but are not exclusive of, salicylates, antipsychotics, sedatives, cholinergics,

Impact of Stratification Based Upon Genotype in Drug Development for Drugs, Compounds, or Candidate Therapeutic Interventions that May Induce CNS Toxicity

There is evidence to suggest that there are safety response differences to drug therapy in reference to development of CNS toxicities which may be attributable to genotypic differences between individuals. There is provided in this invention examples of gene pathways that are implicated in the disease process or its therapy and those that potentially cause this variability. The Detailed Description above demonstrates how identification of a candidate gene or genes and gene pathways, stratification, clinical trial design, and implementation of genotyping for appropriate medical management of a given disease can be used to identify the genetic cause of variations in clinical response to therapy, new diagnostic tests, new therapeutic approaches for treating this undesirable adverse effect, and new pharmaceutical products or formulations for therapy. Gene pathways including, but not limited to, those that are outlined in the gene pathway Tables 1-6, more preferably Table 3, and pathway matrix Table 8 and discussed below are candidates for the genetic analysis and product development using the methods described above.

Advantages of Inclusion of Pharmacogenetic Stratification in Clinical Development of Agents that May Cause CNS Toxicities

As an example of identification of the primary gene and relevant polymorphic variance that directly affects efficacy, safety, or both one could select an gene pathway as described in the Detailed Description, and determine the effect of genetic polymorphism and therapy efficacy, safety, or both within that given pathway. For example, referring to Table 8, genes involved in drug transport, phase I and phase II metabolism, protection from reactive intermediate damage, the optimization of therapy of by an agent known to impart CNS toxic or undesirable side effect or effects by determining whether the patient has a predisposing genotype in which the selected agents are more effective and or are more safe. In considering an optimization protocol, one could potentially predetermine the genotypic profile of these genes involved in the manifestation of the adverse effect, or those genes preeminently responsible for drug response. By embarking on the previously described gene pathway approach, it is technical feasibility to determine the relevant genes within such a targeted drug development program.

Example 20

Drug-Induced Liver Toxicity

Drug-induced liver disease or drug-induced liver toxicity can manifest as zonal necrosis, nonspecific focal hepatitis, viral hepatitis-like reactions, inflammatory or noninflammatory cholestasis, small or large droplet fatty liver, granulomas, chronic hepatitis, fibrosis, tumors, or vascular lesions.

In the majority of the cases of known drug-induced liver toxicity, the drug is metabolized to a form that is deleterious to hepatic, or extrahepatic function. There are many endogenous or exogenous compounds that may be considered to attenuate or ablate toxic hepatocyte-produced metabolite mechanisms or effects of hepatic or extrahepatic damage.

In hepatocellular damage, free oxygen radicals may be generated in the hepatic metabolic processes that are deleterious to intracellular organelles, DNA, or metabolic pathways. There are endogenous cytoprotective agents that may prevent free radical-mediated damage such as retinoids, flavins, reduced glutathione, vitamin E, S-adenylylmethionine, and the enzyme superoxide dismutase (SOD). In animal models in which SOD activity is diminished or absent, the liver function was normal, but the sensitivity to toxin challenge was heightened.

In cholestatic damage, the bile salt uptake, metabolism, secretion, or transport is compromised and the residual increased bile salt concentrations are deleterious to hepatocyte function. The increase in bile salts is the main metabolic

disturbance that initially leads to jaundice and pruritis and can progress to pancreatitis, hyperbilirubinemia, biliary cirrhosis, and hepatic encephalopathy.

In both cases of drug-induced liver toxicity, the drug must first be absorbed and enter in the hepatic circulation. Further, clinically it is often difficult to
5 determine whether cholestatic damage leads to hepatocellular damage or whether hepatocellular damage leads to cholestatic damage. In many cases, until the patient is symptomatic, the underlying damage mechanisms may be clinically overlooked. By the time the drug-induced liver disease is symptomatic, the damage, be it hepatocellular or cholestatic or both, may be irreversible.

Identification of Genes involved in Drug-Induced Liver Toxicity

Thus, in the process of identifying drug- or xenobiotic-induced liver toxicity, one skilled in the art would identify key metabolic enzymes or bile cannicula transport processes that would be linked with either hepatocellular damage or
15 cholestasis or combination of hepatocellular damage or cholestasis.

Hepatocellular damage may be the result of direct chemical mediated effects, may be severe, and usually is associated with damage within organelles, DNA and membranes. Clinically there is a marked elevation of SGOT and SGPT as well as other enzymes. In cases of cholestasis there is jaundice, pruritis, a marked elevation
20 of bile salts and alkaline phosphatase activity, but not an elevation of SGOT or SGPT. In cases of toxic liver disease there is difficulty, at least initially to determine the underlying etiology. Clinically, symptoms may not appear as clear as described above. Further, depending on the rate and extent of the damage, hepatocellular damage may be masked or asymptomatic until liver impairment has induced
25 cholestasis.

Potentially hepatotoxic agents can be divided broadly into two groups: intrinsic hepatotoxins and idiosyncratic hepatotoxins. Intrinsic hepatotoxins produce acute liver damage in a predictable, dose-dependent fashion shortly after ingestion or exposure. Generally, all subjects exposed will uniformly exhibit signs and
30 symptoms. In this category, the effects seen in humans can be mimicked in animal models. Examples of intrinsic hepatotoxins are carbon tetrachloride, 2-nitropropane, trichloroethane, the octapeptide toxins of the *Amanita* mushroom species, and the antipyretic, acetaminophen. In some of these cases, toxic metabolites result in covalent modification of hepatocyte macromolecules or reactive oxygen
35 intermediates leads to peroxidation of cell membrane lipids or other intracellular molecules.

In contrast, idiosyncratic hepatotoxins produce liver damage in an unpredictable, dose-independent manner after a latent period of ingestion or

exposure. Animal models or experimental data is generally incapable of predicting the effect in humans. Further, idiosyncratic hepatotoxins do not uniformly affect a population; a subset of the group exposed may or may not exhibit signs or symptoms. Range of symptoms are from mild to severe and is thought to coincide with differences in the pathways of drug or xenobiotic biotransformation or immune-mediated drug sensitivity (drug allergy). In idiosyncratic drug-induced liver disease, fever, arthralgias, rash, eosinophilia, are often prominent and indicate a hypersensitivity reaction.

Impact of Stratification Based Upon Genotype in Drug Development for Drugs, Compounds, or Candidate Therapeutic Interventions that may Induce Hepatotoxicity

Genes encoding proteins with catalytic function that are involved in the metabolism of drugs or xenobiotics are listed in Tables 3 and 8 below. Further listed are those proteins that are involved in the uptake, transport, or secretion into the bile cannicula. Below are further specific example of drug-specific effects on the liver.

Acetaminophen-Induced Liver Disease

Acetaminophen is a readily available, easy to administer analgesic that is an example of a intrinsic hepatotoxin. This hepatotoxin causes zonal necrosis and acute liver failure and is associated with renal failure. Although a high dose (10-15 grams) is required for significant liver injury to occur, the onset of initial symptoms does not occur until hours after ingestion. The progression of symptoms occurs including progressive liver failure with hepatic encephalopathy, prolongation of prothrombin time, hypoglycemia, and lactic acidosis. The liver injury is caused by a toxic metabolite of acetaminophen via the P450 metabolizing system. This toxic intermediate at low concentrations is conjugated with glutathione. However, in toxic doses, the conjugating enzymes stores are exhausted and the reactive intermediate reacts with intracellular proteins and results in cellular dysfunction and ultimately death. The rate of metabolism is dependent on the concentrations of both P450 and glutathione. Speeding this toxic pathway may include increasing the available P450 or reducing the availability of glutathione, e.g. using known inducers of P450 such as ethanol and phenobarbital; and known inhibitors of glutathione concentrations, e.g., ethanol and fasting. Acetaminophen toxicity is completely reversed if the drug is removed. Chronic ingestion may produce subclinical liver injury, centrilobular necrosis, or chronic hepatitis; however all reversible if the drug is removed.

Amiodarone-Induced Liver Disease

Amiodarone is used in treatment of refractory arrhythmias. In some patients amiodarone produces mild to moderate increases of serum transaminases which are generally accompanied by engorgement of lysosomes with phospholipid. In a fraction of the patients, a more severe liver injury develops which histologically resembles alcoholic hepatitis: fat infiltration of hepatocytes, focal necrosis, fibrosis, polymorphonuclear leukocyte infiltrates, and Mallory bodies. The lesion may progress to micronodular cirrhosis, with portal hypertension and liver failure. Hepatomegaly is seen, but jaundice is rare.

Amiodarone accumulates in lysosomes and inhibits lysosomal phospholipases, however the connection between this mechanism and alcoholic hepatitis histopathology is unknown. Unfortunately, rapid discontinuation of amiodarone increases the risk of cardiac arrhythmias.

Chlorpromazine-Induced Liver Disease

Chlorpromazine is an anti-psychotic agent which, in a small portion of the patient population can produce a cholestatic reaction. Symptoms include fever, anorexia, arthralgias, pruritis, jaundice, and eosinophilia is common. This idiosyncratic type of liver toxicity suggests a hypersensitivity type reaction. The symptoms subside over a period of weeks following discontinuation. Rarely, residual cholestatic disease occurs, treatment for pruritis and fat-soluble vitamin supplementation may be required, but eventual recovery almost always occurs.

Erythromycin-Induced Liver Disease

Erythromycin, a broad spectrum antibiotic, can be accompanied by a cholestatic reaction. Inflammatory cell infiltration and liver cell necrosis may occur. The hepatotoxicity presents as right upper quadrant pain, fever, and variable cholestatic symptoms. The prognosis is uniform and will occur after readministration of the drug. The mechanism of action is unknown.

Halothane-Induced Liver Disease

Halothane is a gaseous anesthetic and can, in rare instances, cause a viral-like hepatitis syndrome. In severe cases, this hepatotoxicity, may cause fatal massive hepatic necrosis. Severe reactions seem to appear after previous or multiple exposure to halothane. It is known that the P450 metabolites of this xenobiotic are responsible for the mechanism of hepatic injury.

Isoniazid (INH)-Induced Liver Disease

Isoniazid is used as a single drug in the prophylaxis of tuberculosis. In 10-20% of the persons taking INH, subclinical liver injury occurs. The conversion of INH to acetylhydrazine is via acetylation. In slow acetylators, INH is more hepatotoxic. The conversion of INH to acetylhydrazine to diacetylhydrazine is impaired. In slow acetylators, the acetylhydrazine is not well metabolized and is further oxidized by one of the P450 enzymes to a toxic, reactive molecule that is responsible for the liver disease. Discontinuation of the drug returns the enzymatic levels to normal and the liver is able to restore activity.

Sodium Valproate-Induced Liver Disease

Sodium valproate is an anti-epileptic agent that is routinely prescribed for petit mal epilepsy and in some cases produces severe hepatotoxicity. Similar to INH, sodium valproate is accompanied by a high incidence of transient, slight and asymptomatic increases in serum transaminases. Usually the increased enzyme activity appears after weeks of treatment. In rare cases of severe liver toxicity, the nonspecific systemic and digestive symptoms are followed by jaundice, evidence of liver failure, as well as encephalopathy and coagulopathy. The mechanism of hepatotoxicity is unknown, however there are theories that there is impairment of mitochondrial oxidation of long-chain fatty acids by a metabolite of the parent drug. Symptoms subside with little to no residual liver dysfunction after discontinuing the drug.

Oral Contraceptive Induced Liver Disease

Estrogen, progesterone, and combination oral contraceptives can produce several adverse effects on the hepatobiliary system. They are 1) hepatocellular cholestasis, 2) liver cell neoplasias, 3) increased predisposition to cholesterol and gall stone formation, 4) hepatic vein thrombosis. These cholestatic hepatotoxic effects are attributed to estrogen's direct effect on bile formation. The mechanism of action is unknown.

There is evidence to suggest that there are safety response differences to drug therapy in reference to development of drug-induced liver toxicity which may be attributable to genotypic differences between individuals. There is provided in this invention examples of gene pathways that are implicated in the disease process or its therapy and those that potentially cause this variability. The Detailed Description above demonstrates how identification of a candidate gene or genes and gene pathways, stratification, clinical trial design, and implementation of genotyping for appropriate medical management of a given disease can be used to identify the genetic cause of variations in clinical response to therapy, new diagnostic tests, new

therapeutic approaches for treating this disorder, and new pharmaceutical products or formulations for therapy. Gene pathways including, but not limited to, those that are outlined in the gene pathway Tables 1-6, more preferably Table 3, and pathway matrix Table 8 and discussed below are candidates for the genetic analysis and product development using the methods described above.

Advantages of Inclusion of Pharmacogenetic Stratification in Clinical Development of Agents that May Cause Liver Toxicity

As an example of identification of the primary gene and relevant polymorphic variance that directly affects efficacy, safety, or both one could select an gene pathway as described in the Detailed Description, and determine the effect of genetic polymorphism and therapy efficacy, safety, or both within that given pathway. For example, referring to Table 8, genes involved in drug transport, phase I and phase II metabolism, excretion, hepatic cannicular uptake and concentration, and protection from reactive intermediate damage the optimization of therapy by an agent known to have a hepatic side effect by determining whether the patient has a predisposing genotype in which the selected agents are more effective and or are more safe. In considering an optimization protocol, one could potentially predetermine the genotypic profile of these genes involved in the manifestation of the adverse effect, or those genes preeminently responsible for drug response. By embarking on the previously described gene pathway approach, it is technical feasibility to determine the relevant genes within such a targeted drug development program.

Example 21

Drug-Induced Cardiovascular Toxicity

Drug induced cardiovascular toxicities include but are not excluded to arrhythmias, tachycardia, extrasystoles, circulatory collapse, QT prolongation, cardiomyopathy, hypotension, or hypertension. Drugs known to elicit these type of responses include but are not excluded to theophylline, hydantoins, doxorubicin, daunorubicin.

Arrhythmias-If the normal sequence of electrical impulse and propagation through myocardial tissue is perturbed, an arrhythmia occurs. Broadly, arrhythmias fall into one of three categories: bradyarrhythmias (slowing or failure of the initiating impulse), heart block (an impaired propagation through node tissue or atrial or ventricular muscle), and tachyarrhythmias (abnormal rapid heart rhythms).

Subcategories include: sinus bradycardia, atrioventricular block (AV block), sinus tachycardia, ventricular tachycardia, atrial flutter, multifocal atrial tachycardia, polymorphic ventricular tachycardia with or without QT prolongation, frequent or

difficult to terminate ventricular tachycardia, atrial tachycardia with or without AV block, ventricular bigeminy, and ventricular fibrillation. Drugs known to induce these types of arrhythmias include, but are not excluded to, digitalis, verapamil, diltiazem, b-adrenergic blockers, clonidine, methyldopa, quinidine, flecainide, propafenone, theophylline, sotalol, procainamide, disopyramide, certain non-cardioactive drugs (), and amiodarone.

Heart Rate, Tachycardia-Heart rate is under both sympathetic and parasympathic control. The influence of heart rate on cardiac output is paramount. Drugs affecting heart rate include, but are not limited to, sympathomimetics, parasympathomimetics, and agents or compounds affecting these two central inputs.

Extrasystoles- is defined as premature myocardial excitation. Extrasystoles can include atrial, nodal, or ventricular. Other asynchronous pathologies may result from these systoles. Drugs known to be associated with extra systoles include, but are not excluded to, agents that prolong the depolarization time, agents that leave a residual available intracellular calcium, or agents that alter the function of the K⁺ or Na⁺ channel activity.

QT Prolongation- is the interval on an electrocardiogram that indicates ventricular action potential duration. QT prolongation can lead to uncoordinated atrial and ventricular action potentials. In these circumstances of delayed or prolonged polymorphic ventricular afterdepolarizations, resultant abnormal triggering of secondary, uncoordinated depolarizations can occur. Two of these conditions are explained as follows and may be associated with underlying rapid or slow heart rate: 1) under conditions of residual excess intracellular calcium (myocardial ischemia, adrenergic stress, digitalis intoxication), and 2) under conditions of marked prolongation of cardiac action potential (agents (antiarrhythmics or others) that prolong action potential duration).

Cardiomyopathy-There are broadly three categories of cardiomyopathies: dilated, hypertrophic, and restrictive. These cardiac muscular diseases can be of mechanical or acquired origin.

Dilated cardiomyopathies are generally caused by myocardial injury that results in depressed systolic function and progressive ventricular dilatation. Drug induced dilated cardiomyopathy can occur in the presence of, but are not excluded to, ethanol, chemotherapeutic agents, elemental compounds, and catecholamimetics.

Hypertrophic cardiomyopathy is the presentation of grossly asymmetric (eccentric) or symmetric (concentric) hypertrophy of the left ventricle in the absence of another cardiac or systemic disease capable of producing the disproportionate increase in ventricle mass. In drug induced hypertrophic cardiomyopathy, there may be compensatory hypertrophy of the left ventricle in response to inordinate and or

sustained hypertension or prolonged reduced or insufficient cardiac output as a result of myocardial injury or noncardiac mediated physiological events.

Restrictive cardiomyopathies are the result of a primary abnormality of diastolic function (impaired filling). Impaired diastolic function can occur as a result of morphologically detectable myocardial or endomyocardial disease, interstitial deposition of abnormal substances (infiltrative), intracellular accumulation of abnormal substances (storage diseases), or as a result of endomyocardial disease. In the last category, anthracyclines have been associated with both dilated and restrictive cardiomyopathies.

Blood Pressure-Blood pressure is regulated in a complex interplay of neural and endocrine mechanisms. These mechanisms are aimed at the physiologic control of cardiac output, delivery of blood components to the tissues, and removal of metabolic by-products from the tissues.

Hypertension is defined as the elevated arterial blood pressure either an increase of systolic or diastolic pressure or both. Secondary hypertension can be associated with drugs and chemicals including, but not limited to, cyclosporine, oral contraceptives, glucocorticoids, mineralocorticoids, sympathomimetics, tyramine, and MAO inhibitors.

Hypotension is defined as the reduction in blood pressure that is associated with orthostatic hypotension, syncope, head injury, hepatic failure, antidiuresis, myocardial infarction and cardiogenic shock. Drug-induced hypotension is associated with drugs including, but not exclusive of, parasympathomimetics, diuretics, and direct acting cardiac agents.

Advantages of Inclusion of Pharmacogenetic Stratification in Clinical Development of Agents that May Cause Cardiovascular Toxicity

As an example of identification of the primary gene and relevant polymorphic variance that directly affects efficacy, safety, or both one could select an gene pathway as described in the Detailed Description, and determine the effect of genetic polymorphism and therapy efficacy, safety, or both within that given pathway. For example, referring to Table 8, genes involved in drug transport, phase I and phase II metabolism, and protection from reactive intermediate damage the optimization of therapy of by an agent known to have a cardiovascular side effect by determining whether the patient has a predisposing genotype in which the selected agents are more effective and or are more safe. In considering an optimization protocol, one could potentially predetermine the genotypic profile of these genes involved in the manifestation of the adverse effect, or those genes preeminently

responsible for drug response. By embarking on the previously described gene pathway approach, it is technical feasibility to determine the relevant genes within such a targeted drug development program.

Example 22

Drug-Induced Pulmonary Toxicity

Drug induced pulmonary toxicity includes, but is not excluded to, asthma, acute pneumonitis, eosinophilic pneumonitis, fibrotic and pleural reactions, and interstitial fibrosis. Drug known to elicit pulmonary toxicity include, but are not excluded to, salicylates, nitrofurantoin, busulfan, nitrofurantoin, and bleomycin.

Advantages of Inclusion of Pharmacogenetic Stratification in Clinical Development of Agents that May Cause Pulmonary Toxicities

As an example of identification of the primary gene and relevant polymorphic variance that directly affects efficacy, safety, or both one could select an gene pathway as described in the Detailed Description, and determine the effect of genetic polymorphism and therapy efficacy, safety, or both within that given pathway. For example, referring to Table 8, genes involved in drug transport, phase I and phase II metabolism, excretion, protection from reactive intermediate damage, and immune responsiveness, the optimization of therapy of by an agent known to have a pulmonary side effect by determining whether the patient has a predisposing genotype in which the selected agents are more effective and or are more safe. In considering an optimization protocol, one could potentially predetermine the genotypic profile of these genes involved in the manifestation of the adverse effect, or those genes preeminently responsible for drug response. By embarking on the previously described gene pathway approach, it is technical feasibility to determine the relevant genes within such a targeted drug development program.

Example 24

Drug-Induced Renal Toxicity

Drug-induced renal toxicity includes, but is not excluded to, glomerulonephritis and tubular necrosis. Drugs associated with eliciting renal toxicity include, but are not excluded to, penicillamine, aminoglycoside antibiotics, cyclosporine, amphotericin B, phenacetin, and salicylates.

Advantages of Inclusion of Pharmacogenetic Stratification in Clinical Development of Agents that May Cause or are Associated with Renal Toxicity

As an example of identification of the primary gene and relevant polymorphic variance that directly affects efficacy, safety, or both one could select an gene pathway as described in the Detailed Description, and determine the effect of genetic polymorphism and therapy efficacy, safety, or both within that given pathway. For example, referring to Table 8, genes involved in drug transport, phase I and phase II metabolism, and renal tubular uptake and concentration the optimization of therapy of by an agent known to have a renal side effect by determining whether the patient has a predisposing genotype in which the selected agents are more effective and or are more safe. In considering an optimization protocol, one could potentially predetermine the genotypic profile of these genes involved in the manifestation of the adverse effect, or those genes preeminently responsible for drug response. By embarking on the previously described gene pathway approach, it is technical feasibility to determine the relevant genes within such a targeted drug development program.

Example 24

Asthma

I. Description of Asthma

Asthma can be an acute or chronic condition associated with inflammation of the lower airways and variable levels of airflow obstruction. Asthma symptoms vary among individuals and may include wheezing, shortness of breadth, tightness of the chest, trouble controlling a cough, persistent cough at night, difficulty breathing during or soon after physical exertion or exercise, or waking up at night due to one of these symptoms. Episodes of these symptoms (referred to as asthma attacks, flare-ups, or exacerbations) occur when there is sufficiently severe airway constriction to render a patient almost unable or unable to breathe. There can be warning signs , however, many attacks are sudden and unanticipated.

Individuals with asthma have inflamed airways that are supersensitive to inducers of asthma which exacerbate asthma and enhance underlying inflammation such as allergens, respiratory infections, or industrial pollutants. Provokers of asthma leading to bronchospasm include exercise or physical activities, irritants, emotions and aspirin. Asthma attacks are associated with swollen and inflamed linings of the airways, excess mucus in the airways, and bronchospasm which are reversible. In chronic asthma, there is persistent activation of resident cells (e.g. basophils, eosinophils, neutrophils) lining the airway leading to chronic inflammation which can result in irreversible changes in the airway pasages. These permanent changes are part of a remodeling process.

Recent evidence has suggested that airway inflammation is a major factor in the pathogenesis and in the severity of the disease. One theory holds that asthma is a T helper 2 (Th2) cell-driven chronic eosinophilia mediated via dendritic and other antigen-presenting cells. The inflammatory nature of the disease is multicellular in nature, with mast cells, eosinophils, macrophages, basophils, lymphocytes, neutrophils, and epithelial cells participating and therefore immunoglobulins, cytokines, chemokines, adhesion molecules, proteinases, inflammatory mediators, and growth factors are involved in various stages and interact to maintain and amplify the inflammatory response. The net result of these interactions is persistent inflammation and repair, ultimately leading to irreversible airway remodeling.

II. Current therapies for Asthma

Because asthma results from a complex combination of mediators of inflammation, most useful anti-asthma agents affect pathways for these mediators. In acute or chronic asthma, the therapeutic categories include: immunosuppressive agents including glucocorticoids, antiinflammatory agents including leukotriene receptor agonists and mast cell stabilizers (cromolyn sulfate); bronchodilators including β -adrenergic agonists, sympathomimetic agents, and xanthines; and agents to treat cough and excess mucus including expectorants and mucolytics.

Corticosteroids affect the inflammation within the airways by decreasing growth and development of mast cells, inducing apoptosis, suppressing lymphocyte generation of IL-5 and other cytokines, inhibiting some mediator release, inhibiting cytokine production, inhibiting the transcription of cytokines (for example IL-8, TNF- α , prototypic antiviral chemokine (regulated-on-activation normal T-expressed and secreted, RANTES), and GM-CSF), and inhibiting nitric oxide synthesis.

β -Adrenergic agonists and sympathomimetics affect the pulmonary airway lining in a well-characterized mechanism of β -adrenergic receptor activation of adenylyl cyclase as well as cAMP independent mechanisms. Bronchodilation is the immediate clinical effect.

Leukotriene modifiers affect the airway by inhibition of 5-lipoxygenase, the initial enzyme of leukotriene biosynthesis, and exert their effect by decreasing leukotriene production, thereby interfering with eosinophil migration and other processes.

Corticosteroids affect the inflammation within the airways by decreasing growth and development of mast cells, inducing apoptosis, suppressing lymphocyte generation of IL-5 and other cytokines, inhibiting some mediator release, inhibiting cytokine production, inhibiting the transcription of cytokines (for example IL-8,

TNF- α , prototypic antiviral chemokine (regulated-on-activation normal T-expressed and secreted, RANTES), and GM-CSF), and inhibiting nitric oxide synthesis.

Corticosteroids in combination with long-acting β -adrenergic agonists work well as combination therapy.

5 Cromones are believed to act on the airway by modifying mediator release, and inhibiting mast cell degranulation.

Xanthines are believed to act on the airway in asthma by inhibiting eosinophil cell migration, and enhancing β -adrenergic pathway mediated bronchodilation via the inhibition of phosphodiesterase.

10 Difficult to treat or therapy-resistant asthma syndromes present a challenge to clinicians. They include difficult acute and chronic, as well as chronic severe, acute severe, therapy-resistant, difficult to control and corticosteroid-dependent asthma.

15 *III. Limitations of Current Therapies for Asthma*

Limitations Involving Efficacy

The therapies discussed above do not reverse the underlying pathological process in asthma; they merely slow or retard the progression of asthma. As thickening of the airways occurs and becomes irreversible the therapeutic options
20 become limited. Thus, therapies for asthma are aimed at reduction of inflammatory processes and control of symptoms starting at the earliest date (frequently in the pediatric setting).

The limitations of the adrenergic agonist compounds used for the treatment of asthma include short duration of action and ligand desensitization. Excessive use of
25 short acting β -adrenergic agonists has been proposed to lead to loss of asthma control and consequent increases in morbidity and mortality. Long acting bronchoactive/bronchoprotective agonists acting at adrenergic receptors have supplanted short duration β -agonists.

30 Short-acting β -adrenergic agonists are primarily used for the relief of acute asthma symptoms. Excessive reliance on these agents is generally not advisable because 1) β -adrenergic receptors undergo a rapid desensitization and the agonist becomes an ineffective bronchodilator, and 2) repetitive high doses of short acting β -adrenergic agonists may be detrimental to the control of asthma by potentially interfering with corticosteroid action. This desensitization occurs through a process
35 involving G-protein receptor coupled-kinases and or cAMP dependent protein kinase or by enhanced degradation of cAMP by phosphodiesterase activity.

Glucocorticoid associated side effects include increased appetite, weight gain, fluid retention, acne, ecchymosis, development of Cushingoid facies,

hypertension, hyperkalemia, diabetes, hyperglycemia, hyperosmolar state, hyperlipidemia, hepatic steatosis, atherosclerosis, myopathy, aseptic necrosis, osteoporosis, ulcers, pancreatitis, psuedotumor cerebri, psychosis, glaucoma, cataract formation, vascular necrosis, increased suseptibility to infection, impairment of the hypothalamus-pituitary axis, decreased thyroid hormone serum binding protiens, and impaired wound healing.

Theophylline or other phosphodiesterase inhibitors have been shown to have a narrow therapeutic window and can result in life-threatening cardiac arrhythmias.

Difficult to treat asthma involves a spectrum of disease that responds suboptimally to doses of glucocorticoids. In the face of partial response to inhaled or oral steroids, higher doses are administered risking steroid associated side-effects.

The reduction of clinical symptoms of asthma following antiinflammatory therapy may only become evident after several weeks to months of therapy. The slow action of these therapies creates problems for the clinician seeking to expeditiously determine optimal therapy for an individual patient. The development of genetic tests to predict response to different agents will allow selection of optimal therapy with less of the time consuming empirical clinical decision making required presently.

Limitations Involving Toxicity or Undesired Side Effects

There are toxicities and undesired side effects associated with the above current therapies for asthma that require monitoring. Drugs used to treat asthma may cause death, disability, disease, and place a fetus at risk. The undesired side effects or toxicities are listed for each drug category as described above.

IV. Impact of Stratification Based Upon Genotype in Drug Development for Drugs, Compounds, or Candidate Therapeutic Interventions for Asthma

In a recent report, it was demonstrated that the 5-lipoxygenase (5-LO) gene promoter variation among asthma patients is linked to drug response to 5-LO inhibitors (Drazen et al., Nature Genetics 22: 1999). In a clinical trial to test efficacy of a potent, selective 5-LO inhibitor (ABT-761), the trial was abruptly closed due to inordinate event rate of abnormal liver function tests. Although the projected enrollment was not reached, the interim data suggested superior efficacy regarding forced expiratory volume in the high dose relative to low dose or placebo groups. The investigators chose to stratify the high dose and placebo group of the enrolled patients based upon genotype of the 5-LO gene promoter. The 5-LO gene promoter has been found to contain 3-6 tandem repeats of the Sp1-binding motif. The wild-type allele was designated as 5 tandem repeats and had a frequency of

0.772 in the study population. The forced expiratory volume data indicated that heterozygous patients on high-dose active treatment had, on average, an improvement of forced expiratory volume within one week ($23.3 \pm 6.0\%$) and was similar to the wild-type patients ($18.8 \pm 3.6\%$). In contrast, the patients with mutant genotype had no benefit from active 5-LO inhibitor treatment ($-1.2 \pm 2.9\%$). In the table below, the trial outcome data is described for two periods following treatment with high dose or placebo.

Patient Group	FEV ₁ , % change from baseline ^a	
	Day 8	Day 84
Wild type, high dose	8.2	18.5
Mutant, high dose	1.8	5
Placebo	-0.7	-1.4

^aData extrapolated from published data

Approximately 6% of asthma patients do not carry a wild-type allele at the 5-LO core promoter locus, and this data indicates that these patients would not benefit from 5-LO inhibitor drug therapy. Further, these data indicate that there is evidence to reasonably identify patients, i.e. stratification based upon 5-LO genotype, to appropriately treat patients with asthma.

A recent double blind, placebo controlled crossover designed pharmacogenetic retrospective clinical trial of a β 2-adrenoreceptor polymorphism was implemented to analyze the significance of β 2-adrenoreceptor polymorphisms (Tan et al. Lancet 350:995-999). *In vitro* studies have suggested that polymorphism of the β 2-adrenergic receptor may influence the desensitization induced by β 2 agonists. Twenty two moderately severe asthmatics were enrolled into a placebo controlled cross-over study of formoterol (a β 2-adrenergic agonist). The patients were divided into groups by allelic variances: 1) at codon 16, homozygous arginine (n=4), heterozygous arginine/glycine (n=8), and homozygous glycine (n=10); and 2) at codon 27, homozygous glutamine (n=5), heterozygous glutamine/glutamic acid (n=11), and homozygous glutamic acid (n=6). Genotypic analysis determined that individuals who were homozygous for glycine at codon 16 were also homozygous for glutamic acid at codon 27. The results were as follows:

Polymorphisms of the β 2-adrenergic	Degree of Brochodilator Desensitisation after Formoterol Therapy ¹			
	6 hour FEV ₁	Maxim al FEV ₁	6 Hour FEF ₂₅₋₇₅	Maxim al

receptor				FEF ₂₅₋₇₅
Gly 16 (n=10)	80%	48%	103%	73%
Arg 16 (n=4)	28%	-8%	23%	-35%
Gly/Arg16 (n=8)	57%	48%	70%	50%
Glu27 (n=6) ²	73%	35%	90%	68%
Gln27 (n=5)	47%	3%	38%	-15%
Glu/Gln27 (n=11)	65%	52%	70%	45%

¹Data extrapolated from published graphs.

²All individuals homozygous for Glu27 were also homozygous for Gly16.

The homozygous glycine at position 16 was associated with individuals who were prone to bronchodilator desensitization than at arginine at position 16: the mean FEV₁ desensitisation was 80% for Gly16 homozygotes versus 28% for the Arg16 homozygotes. Similar results were observed for the 6 hour FEV₁ and the FEF.

For the polymorphism at codon 27, the mean for the Glu27 homozygous individuals demonstrated greater desensitization than those who were homozygous for Gln27.

The allelic variance, glycine at position 16 appeared to dominate over the putative protective effects of the mutation of glutamic acid at position 27.

The effects of the codon 16 and 27 polymorphism in the β 2-adrenoreceptor on β 2-agonist desensitization, as observed in the above data, suggest that there may be an identifiable subset of patients for whom β 2-adrenergic receptor desensitization occurs in the presence of long-acting or repeated use of β 2-agonists.

Thus, one skilled in the art, will be able to utilize the presently described pharmacogenetic techniques to identify the allelic variances with the coding region of the β -adrenergic receptor or other receptor proteins that are similar to the β -adrenergic receptor, including but not limited to those variances for those genes listed in Tables 4, 15, and 21 and those 7-membrane spanning receptor G-protein coupled receptors. In this way, a skilled practitioner will be able to utilize the methods, protocols, and techniques that are described in the detailed description and those known in the art to identify the gene targets, allelic variance or variances, and candidate drugs that affect these pathways. Further, one can design and implement a strategy that incorporates a diagnostic test to genotype the individual for a given allele or alleles or haplotype, grouping these candidates by genotype, and testing a β -adrenergic agonist or other candidate therapeutic product for the affect of the pharmacogenomic difference between or among the groups.

As described above, there is evidence to suggest that there are safety response differences to drug therapy in asthma which may be attributable to genotypic differences between individuals. There is provided in this invention examples of gene pathways that are implicated in the disease process or its therapy and those that potentially cause this variability. The Detailed Description above demonstrates how identification of a candidate gene or genes and gene pathways, stratification, clinical trial design, and implementation of genotyping for appropriate medical management of a given disease can be used to identify the genetic cause of variations in clinical response to therapy, new diagnostic tests, new therapeutic approaches for treating this disorder, and new pharmaceutical products or formulations for therapy. Gene pathways including, but not limited to, those that are outlined in the gene pathway Tables 1-6, preferably Table 4, and pathway matrix Table 9 and discussed below are candidates for the genetic analysis and product development using the methods described above.

As an example of identification of the primary gene and relevant polymorphic variance that directly affects efficacy, safety, or both one could select an gene pathway as described in the Detailed Description, and determine the effect of genetic polymorphism and therapy efficacy, safety, or both within that given pathway. For example, referring to Table 9, genes involved in cytokine-mediated immune regulation, non-cytokine mediated immune regulation (including, but not excluded to, cyclophilins, corticosteroids), cell mediated inflammation involving apoptosis, adhesion and migration, protease and protease inhibitors, complement, degranulation (platelets, mast cells, neutrophils, and eosinophils), release of inflammatory modulators (including membrane lipids, prostaglandin, platelet activating factor, leukotrienes, histamine, nitric oxide), vascularization mediators (including endothelin and vascular endothelial cell growth factor), neurotransmitters and peptide hormone inflammation modulators (including adrenergic, purinergic, cholinergic, ion channels, tachykinin, neurokinin, substance P, bradykinin, parathyroid hormone, melanocortin and adrenocorticotrophic hormones, and modulators of general cell growth pathways the optimization of therapy of by an agent can be achieved by determining whether the patient has a predisposing genotype in which the selected agents are more effective and or are more safe. In considering an optimization protocol, one could potentially predetermine the genotypic profile of these genes involved in the manifestation of the adverse effect, or those genes preeminently responsible for drug response. By embarking on the previously described gene pathway approach, it is technical feasibility to determine the relevant genes within such a targeted drug development program.

Description of Mechanism of Action Hypotheses for Future Drug Development

There are many potential mechanisms that may serve as targets for candidate therapeutic interventions. For example, phosphodiesterase inhibitors to PDE4; T-lymphocyte-eosinophil interactions inhibition: targeting the factors involved in the regulation of the TH2(CD+4) differentiation and/or activation by soluble factors (cytokines (IL-4, IL-5); co-stimulatory molecules (B7-2/CD86); and transcription factors (GATA-3, AP-1). These targets may be available to limit the TH2 cell involvement in the initiation of asthmatic inflammation.

Suppression of eosinophil adhesion with consequent inhibition of influx into the lung is a strategy to suppress asthmatic airway inflammation. Such inhibition may be mediated through inhibitors directed towards very late antigen-4 (VLA-4), monoclonal antibodies directed towards VLA-4, intracellular adhesion molecule 1 (ICAM1), and alpha 1,3-fucosyltransferase VII (an enzyme which regulates selectin function). Furthermore, molecules may be targeted to suppress the expression of adhesion molecules (e-selectin, vascular cell-adhesion molecule 1 (VCAM-1), and ICAM1).

There are a group of chemokines that contain a cysteine-X-cysteine motif, such as IL-8 that are effectors of acute inflammatory episodes, whereas cysteine-cysteine chemokines, such as macrophage inhibitory peptide 1 (MIP-1), eotaxin, RANTES, or macrophage chemotactic peptide 1 (MCP-1) act as chronic mediators of inflammation. These molecules may be appropriate targets for inhibiting either the acute or chronic inflammatory pathway.

Cysteinyl leukotrienes have a central role in the development of chronic asthma, and antagonists (i.e., CysLT₁) may be able to ablate the actions of this ligand. These novel leukotriene receptor agonists may have potential for anti-inflammatory effects. Endothelin receptors may also be a target, with endothelin antagonists to specific receptor subtypes ET_A or ET_B. Other receptors known to be involved in the inflammatory process that may be potential targets are the tachykinin NK1 receptors and selective ligands to the NK1/NK2 receptors.

Induction of cyclooxygenase and the consequent increase in prostaglandin release is associated with the development of inflammation. Antisense oligonucleotides directed against the receptor types NK-kB, major basic protein, 5-lipoxygenase, leukotriene C4(LTC4 synthetase, IL-4, IL-5, IL-8 and adenosine have been developed that are inhalable products that can directly block the expression of these mediators of the inflammatory response.

Other areas of drug target development include immunobiology of the airways i.e., TH1 and TH2 and their involvement in the immune response, synthesis of immunoglobulin, IgE, integrins, inhibition of α IL5 and α IL5 monoclonal

antibody, soluble IL4 receptor, neurokinin receptor antagonist, chemokine inhibitors.

5 The inflammatory response is also being evaluated in terms of the effects of NO₂, SO₂, and ozone on the subsequent effect on airway response to these potential allergens. As well as adhesion molecule expression, cytokine production, and cytokine gene transcription factors.

10 Optimization of nonsteroidal or steroidal antiinflammatory agents, or agents aimed at a mechanism of therapy of the underlying etiology of asthma further demonstrates the utility of selection of a potential asthma patient that has a predisposing genotype in which selective antiasthmatic or other agents may be more effective and or have an more desirable safety profile. In considering an optimization protocol, one could potentially predetermine variance or variances within the nonsteroidal antiinflammatory pathway, steroid antiinflammatory pathway, or antiinflammatory mediated intracellular mechanism of action that is preeminently responsible for antiasthmatic drug response. By embarking on the previously described gene pathway approach, it is technically feasible to determine the relevant genes within such a targeted drug development program for asthma.

15 A sample of therapies approved or in development for preventing or treating the progression of asthma currently known in the art is shown in Table 47. In this table, the candidate therapeutics were sorted and listed by mechanism of action. Further, the product name, the pharmacologic mechanism of action, chemical name (if specified), and the indication is listed as well.

Example 25

Inflammatory Bowel Disease

Description of Inflammatory Bowel Disease

25 Inflammatory bowel disease (IBD) is a broad clinical term that includes idiopathic chronic inflammatory bowel diseases including Crohn's disease (CD) and ulcerative colitis (UC) which can be distinguished from inflammatory bowel disease of known origin including diverticulitis, radiation enteritis, colitis, drug or toxin-induced enterocolitis, or vasculitis of the intestinal tract. UC is a term that encompasses a broad category of diffuse, continuous, and superficial inflammation of the colon, which begins within the rectum and extends proximally. The condition is limited to the colon and large intestine, with limited involvement of the small intestine. In UC, the inflammation primarily affects the mucosal process and is not transluminal within these anatomical regions. CD is characterized by focal, asymetric, transmural inflammation affecting any portion of the gastrointestinal tract, i.e. from the mouth to the anus. The focal localization and possible extent of the

inflammation distinguishes UC from CD. There are currently approximately 35-100 and 10-100 CD per 100,000 Americans diagnosed with UC or CD, respectively.

Clinically, patients with UC experience variable stool consistencies from constipation to diarrhea, low-grade fever, malaise, nausea, vomiting associated with defecation, night sweats, arthralgias, dehydration, tachycardia, and symptoms of abdominal tenderness. There can be rectal bleeding, tenismus, and passage of mucus.

Patients with Crohn's disease experience symptoms of peptic ulcer disease, nausea, vomiting, and epigastric pain. Transmural inflammation leads to fibrosis and transluminal narrowing. In some cases, the narrowing leads to signs and symptoms of intestinal obstruction including nausea, vomiting, waves of abdominal pain, and a reduced output of stool. Patients with colonic CD are likely to experience abdominal pain, cramping or localized pain, rectal bleeding, and diarrhea. Weight loss is common among CD patients due to malabsorption of nutrients and reduced food intake due to minimization of postprandial symptoms.

There are extraintestinal manifestations of inflammatory bowel disease affecting the following processes including: nutritional and metabolic abnormalities, hematologic abnormalities, skin and mucous membranes, musculoskeletal, hepatic and biliary abnormalities, renal complications, and optic complications. These complications are associated when the colon or intestinal tract is inflamed. These complications are clinically manifested as joint swelling or pain, erythema nodosum, pyoderma gangrenosum, sclerosing cholangitis, conjunctivitis, or uveitis.

There is an increased risk for the development of gastrointestinal cancer in patients with IBD. In both UC and CD, there is an increased risk of adenocarcinoma of the intestine. This is not correlated to the intensity of the first attack, subsequent course, or any specific medical therapeutic approach. Therefore routine screening for dysplasia and neoplasia is warranted.

Current Therapy of Inflammatory Bowel Disease

Strategies for the therapy of inflammatory bowel disease includes antiinflammatory agents, and immunomodulation.

Antiinflammatory agents include the use of glucocorticoids and the aminosalicylates. Glucocorticoids act by modulation of the immune response. Corticosteroids affect the inflammation within the gastrointestinal tract by decreasing growth and development of mast cells, inducing apoptosis, suppressing lymphocyte generation of IL-5 and other cytokines, inhibiting some mediator release, inhibiting cytokine production, inhibiting the transcription of cytokines (for example IL-8, TNF- α , prototypic antiviral chemokine (regulated-on-activation

normal T-expressed and secreted, RANTES), and GM-CSF), and inhibiting nitric oxide synthesis.

5-aminosalicylic acid (5ASA) is a salicylate that is used for the treatment of IBD, is not orally active, is poorly absorbed and is inactivated by intestinal bacteria, and is delivered as a suppository or rectal suspension enema. Oral formulations can be used to deliver active drug to the lower intestine which are cogeners of 5ASA. The aminosalicylates are potent antiinflammatory agents that inhibit cyclooxygenase (COX), a rate limiting enzyme in the prostaglandin and leukotriene pathway.

Immunosuppressive agents are also used to modulate the inflammatory/immune response. There are four broad categories of immunosuppressive agents that have distinct mechanisms of action: inhibition of ribonucleotide synthesis which acts to inhibit the proliferation of T-cell clones (6-mercaptopurine), inhibition of folic acid which acts to inhibit T-cell and B-cell function as well as decrease IL-1 and IL-6 activity (methotrexate), inhibition of T-cell receptor stimulated transcription of lymphokine genes which act to inhibit the production of IL-2 and IL-2 receptors as well as inhibit certain cytokines (TNF- α , IFN- γ) (cyclosporin and FK506), and inhibition of guanosine nucleotide synthesis which acts as cytostatic effects on lymphocytes (mycophenolate). Each of these categories of agents have been employed for the therapy of IBD.

Recently a chimeric monoclonal antibody was approved for use in the treatment of moderately to severe active Crohn's disease for those patients that are unresponsive to conventional therapy. This monoclonal antibody is specific for TNF- α and can remove TNF from the bloodstream before it reaches the site of inflammation.

Crohn's disease may progress to a level and extent in which surgical removal of the localized inflammation is warranted. Surgery has been indicated for recurrent intestinal obstruction, complicated fistulas, intractable hemorrhage, disease refractory to medical therapy, growth retardation refractory to therapies, or cancer. The surgical procedures vary from excision of a localized, diseased portion of the gastrointestinal tract to removal of large portions, i.e. the entire colon (colectomy). Surgical excision of the inflamed region or to correct complications such as blockage, perforation, abscess, or bleeding can result in a substantial relief of symptoms.

Limitations to Current Therapies for IBD

Salicylate associated side effects include dyspepsia, gastric or small bowel bleeding, ulceration, renal insufficiency, confusion, rash, headache, hepatic toxicity. NSAIDs also reversibly inhibit platelet aggregation and prolong bleeding time.

Glucocorticoid associated side effects include increased appetite, weight gain, fluid retention, acne, ecchymosis, development of cushoid facies, hypertension, hyperkalemia, diabetes, hyperglycemia, hyperosmolar state, hyperlipidemia, hepatic steatosis, atherosclerosis, myopathy, aseptic necrosis, osteoporosis, ulcers, pancreatitis, psuedotumor cerebri, psychosis, glaucoma, cataract formation, vascular necrosis, increased suseptibility to infection, impairment of the hypothalamus-pituitary axis, decreased thyroid hormone serum binding protiens, and impaired wound healing.

Agents involved in immunomodulation have the following undesirable side effects including antimetabolites: hepatic compromise including hepatic fibrosis, ascites, esophageal varices, cirrhosis, pneumonitis, myelosuppression; immunosuppressives: myelosuppression, (cyclosporine: renal insufficiency anemia, hypertension.

Monoclonal antibody to TNF proteins therapies have been shown to generate a human-antimouse antibody response (HAMA). However, patients on immunosuppressive agents such as glucocorticoids and others are less likely to generate antibodies to the treatment antibody. Delayed hypersensitivity is demonstrable 2 to 4 years after initial treatment in 25% of the patients treated with the chimeric antibody. Further, there are patients that develop a serum sickness reaction which includes fever, and joint swelling that requiring hospital admission. A positive antinuclear antibody (ANA) occurred in 24-36% of the patients analyzed. Nine percent of the patients developed anti-DNA antibodies, less than 1% developed a lupus-like reaction requiring steroid therapy.

In surgical therapy of IBD, reccurring inflammation and relapse, after excision procedures occurs in 75% of the patients. Attempts have been made to include salicylate therapy after resective surgery, however, the inflammation reccurance rate in that group was 52%.

Impact of Stratification Based Upon Genotype in Drug Development for Drugs, Compounds, or Candidate Therapeutic Interventions for Autoimmune Disease Thiopurine methyltransferase (TPMT)

The thiopurine S-methyltransferase (TPMT) is a cytosolic enzyme whose precise physiological role is unknown. This enzyme catalyzes the S-methylation of widely used immunosuppressive or cytotoxic thiopurine drugs such as 6-thioguanine, 6-mercaptopurine and azathioprine.⁸ The *in vivo* activity of this cytosolic enzyme is characterized by interindividual and interethnic variability caused by the genetic polymorphism of the TPMT gene, which was discovered, using pharmacogenetic techniques, by the existence of three major phenotypes, high

(HM), intermediate (IM) and deficient (DM) methylation. As a consequence, individuals greatly differ in detoxication of thiopurine drugs to 6-methylmercaptopurine as well as the occurrence of side effects or therapeutic efficacy. Using genomic techniques, PCR-SSCP (polymerase chain reaction – single strand conformation polymorphism), Spire-Vayron de la Moureyre et al. 9 have defined the mutational and allelic spectrum of TPMT in a group of 191 Europeans. In this analysis, PCR-SSCP techniques identified allelic variances in the entire coding sequence, the exon-intron boundaries, the promoter region and the 3'-flanking region of the genes. Six mutations were detected throughout the ten exons and seven TPMT alleles were characterized. Within the promoter region, six alleles 10 corresponding to a variable number of repeats (VNTR) were identified. The TPMT phenotype was correctly predicted by genotyping for 87% of individuals. A clear negative correlation between the total number of repeats from both alleles and the TPMT activity level was observed, indicating that VNTRs contribute to inter- 15 individual variations of TPMT activity. This VNTR polymorphism can be considered responsible for shifts to lower or higher TPMT activities observed among discordant individuals. Seven out of the nine phenotyped HMs but genotyped IMs were carrier of a total of eight VNTR repeats. This low number of repeat can account for the switch to high TMPT activities of these samples.

20 One in 300 patients with IBD are homozygous-deficient for TPMT. The clinical relevance for this deficiency is that TPMT is the enzyme responsible for the conversion of 6-MP to 6-MMP, and the AZA compounds to 6-TG. In TPMT deficient patients, higher levels of 6-TG and 6-MMP are then produced and are associated with significant leukopenia. In general, patients produce variable levels 25 of 6-TG and 6-MMP as determined by their intrinsic enzyme systems. Higher 6-TG levels are correlated with good therapeutical response, but produce leukopenia. Higher 6-MMP levels correlate with hepatotoxicity and in recent studies with leukopenia.

30 There is evidence to suggest that there are safety response differences to drug therapy in IBD which may be attributable to genotypic differences between individuals, one example being the TPMT gene described above. There is provided in this invention examples of other gene pathways that are implicated in the disease process or its therapy and those that potentially cause this variability. The Detailed Description above demonstrates how identification of a candidate gene or genes and 35 gene pathways, stratification, clinical trial design, and implementation of genotyping for appropriate medical management of a given disease can be used to identify the genetic cause of variations in clinical response to therapy, new diagnostic tests, new therapeutic approaches for treating this disorder, and new pharmaceutical products

or formulations for therapy. Gene pathways including, but not limited to, those that are outlined in the gene pathway Tables 1-6, preferably Table 4, and Table 9 and discussed below are candidates for the genetic analysis and product development using the methods described above.

5
V. *Description of Mechanism of Action Hypotheses for Future Drug Development*

The majority of the hypotheses for future therapeutic interventions for inflammatory bowel disease are based upon the understanding the immunologic mechanisms that cause and perpetuate the inflammation within the gastrointestinal tract. Although the initiating event is elusive, the resulting immunologic events have been studied. All of the gastrointestinal enterocytes have immunologic function. Under physiologic conditions, these enterocytes selectively activate CD8+ nonspecific suppressor cells, in response to inflammation. In patients with IBD, these enterocytes selectively stimulate the development of CD4+ helper T cells which can respond in two ways 1) the Th1 response which involves the activation of IL-2 and IFN-g and leads to delayed hypersensitivity and cellular immunity and 2) the Th2 response which involves IL-4, IL-5, IL-6, and IL-10 and leads to antibody response and humoral immunity. Both Th1 and Th2 responses are genetically controlled and are coordinately regulated, i.e. Th1 response stimulation results in down regulation of Th2 response and vice versa. It has been demonstrated that in UC patients the Th2 response is favored and in CD patients the Th1 response is favored.

25 A humanized (95% human, 5% mouse) version of the chimeric antibody (75% human, 25% mouse) to TNF is currently under development. Some antiidiotypic antibodies are generated, but it doesn't appear to stimulate a delayed hypersensitivity, no stimulation of anti-DNA antibodies, or lupus-like reactions.

Mediators of the immune response including intracellular adhesion molecule (ICAM-1) inhibitors (antisense molecules or others), IL-10, IL-11 have been tested in humans. Further, and anti-CD4 monoclonal antibody which has been shown to interfere with the interaction of the CD4 molecule and the HLA class II molecules leading to an inhibition of antigen presentation has been tested.

Thalidomide (inhibitor of TNF, acceleration of the degradation of the TNF mRNA) is also under consideration.

35 It has been noted that individuals who smoke tobacco products have a lower incidence of IBD. Therefore, understanding the immune response and correlation with nicotinic chloinerbic pathways is under investigation.

A sample of therapies approved or in development for preventing or treating the progression of IBD currently known in the art is shown in Table 48. In this table, the candidate therapeutics were sorted and listed by mechanism of action. Further, the product name, the pharmacologic mechanism of action, chemical name (if specified), and the indication is listed as well.

Example

Hepatitis C

Selecting Optimal Therapy for HCV Patients

Genetically Determined Variation in Response to Interferon α

Treatment of hepatitis C virus (HCV) infection with interferon α is expensive, benefits a minority of patients, and produces side effects in a significant fraction of patients. Addition of ribavirin increases efficacy, but combination therapy remains expensive and still falls well short of providing a lasting benefit to most patients. It would therefore be desirable to identify prospectively those patients likely to have a sustained response to treatment. Ideally a diagnostic test would also predict what dose of interferon and ribavirin, administered for what length of time, will afford to each patient the best chance of a sustained response. Pre-treatment identification of patients likely to suffer serious toxic side effects would also be desirable.

The best characterized predictors of response to interferon α therapy are viral load and HCV genotype. Low viral load before therapy is predictive of a positive response. However, demonstration of decreased viral load after initiation of therapy is currently the best predictor of response to therapy. There is no consensus on the optimal time after initiation of therapy for measuring viral levels; periods ranging from 2 weeks to four months have been proposed. The viral load test is not very effective at discriminating long term responders from those patients who suffer rebound of HCV infection within 6 months after treatment. Also, the ideal test would be performed in advance of any treatment, thereby saving the considerable costs associated with even short term therapy. In search of other predictive indices, over 100 controlled clinical studies have examined a variety of viral and host factors in responders and nonresponders. Genetic variation in both HCV and host genes has been shown to independently influence patient response to interferon α treatment. A consensus has emerged regarding the interaction of viral genotype and treatment response, however the contribution of host factors to treatment response has not been as well investigated. There are a number of promising recent findings suggesting that polymorphisms in regulators of human immune function are correlated with response to interferon α .

Viral genome variation

Comparison of sequenced HCV genomes reveals considerable variation in viral sequence, with at least 6 major types and well over a dozen minor types recognized. The geographical distribution of viral types is nonrandom, perhaps accounting for some of the apparent racial heterogeneity in the natural history of HCV infection. HCV is present in each patient as a heterogeneous population of viral quasispecies, with the degree of heterogeneity differing among patients. Despite these complexities, there are strong correlations between predominant viral type and treatment response. In general, patients with genotype 1 (especially 1b) respond poorly to interferon α , with many studies showing response rates under 10 percent. Patients with genotype 2 or 3 do well, with response rates typically greater than 40 percent. Most viral genotyping is based on a short variable segment, however there are multiple segments of the viral genome that vary, and some studies have found that more detailed viral genotyping, for example of the 5' untranslated region, provides stronger correlations with treatment response.

Human genome variation

A recent study suggests that there is significant variation in response to interferon α treatment among racial groups in the US, even after controlling for the effect of different HCV types. This finding suggests that host genetic variation may be an important factor in response. A number of candidate genes have recently been tested for correlation with interferon α response. The best studied genes are regulators of immune function such as IL-6, IL-10 and TNF α . One study, for example, found that patients with high expression of IL-10 (attributable to a specific haplotype) tend to respond poorly to interferon, perhaps due to impaired immune response. IL-4, IL-12 and TGF- β levels have been correlated with treatment response in some (but not all) studies, however no genetic analysis has been performed. Similarly, hepatic levels of interferon α - β receptor have been correlated with response to interferon, but no genetic analysis has been performed to determine whether polymorphism affects receptor levels. HLA alleles have also been correlated with response to interferon, particularly the A24-B54-DR2 haplotype. A number of other compelling candidate genes have not been investigated. For example, a recent report shows that HCV can enter cells via the low density lipoprotein receptor. If so, the well studied amino acid polymorphisms of the LDL-R should be investigated for effects on disease course and response to treatment. There are also likely to be genetic factors that influence response to ribavirin; for example, the drug must be transported across the plasma membrane and then

phosphorylated before becoming a substrate for viral enzymes. The transporters and kinases responsible for these processes may be worth genetic investigation.

An optimal test for selecting treatment for HCV infection would (i) suggest the optimal therapeutic regimen (interferon alone, interferon and ribavirin, or some other combination), (ii) suggest the optimal dose and duration of treatment, (iii) predict sustained responders vs. short term responders, and (iv) predict patients likely to suffer serious adverse effects. At least three areas should be further investigated to better predict the response to interferon α treatment. First, it is not clear that conventional viral genotyping methods, focusing on the 5' untranslated region, capture all of the aspects of viral sequence variation that affect viral biology. Additional genetic determinants of viral pathogenicity should be investigated. Second, the human gene variants that have been associated with response need to be more thoroughly investigated, and interactions between human candidate gene alleles, as well as perhaps between human genes and viral genes, should be tested. Third, recent work suggests a number of new host proteins that may affect response to interferon, and proteins that mediate response to ribavirin have not yet been investigated. The genes encoding these proteins should be thoroughly investigated. With additional information on candidate genes available it should be possible to construct a plan, ideally via retrospective analysis of clinical trial data, for first assessing the impact of variation in each of the candidate genes, then examining gene x gene interactions, and finally reducing the number of tests to a much smaller number for confirmatory prospective trials.

In Table 49, there a list of the candidate therapeutic interventions that in development for Hepatitis. One skilled in the art could apply, as described in the text, the methods of this invention to ascertain whether there is a gene in the inflammatory pathway that may be involved in the efficacy, safety, or toxicities of these candidate interventions.

Example 27

Pro12Ala Substitution in PPAR γ 2 Affects Insulin Sensitivity

Peroxisome proliferator-activated receptors (PPARs) are members of the nuclear hormone receptor family of DNA binding transcription factors. PPARs form heterodimers with retinoid X receptors and the resultant heterodimers, in coordination with coactivators and corepressors, bind to DNA and activate transcription of various genes. The PPAR superfamily includes receptors that mediate the size and number of peroxisomes in response to a diverse group of chemicals both naturally occurring and xenobiotics. Endogenous ligands thought to activate the PPARs are arachidonic acid, oleic acids, andogenous molecules (fatty

acids or steroids), C18 unsaturated fatty acids, peroxisome proliferation activators, and others (see Table 5). Diverse chemicals can activate the PPARs: herbicides, leukotriene antagonists, plasticizers (phthalate ester plasticizers used in the production of vinyl plastics), the fibrate class of hypolipidemic agents, thiazolidinediones. Overstimulation of these receptors can result in hepatomegaly, liver hyperplasia, and possibly hepatocellular carcinoma. There are three known PPARs, α , γ , δ . PPAR α is believed to be involved in the regulation and control of fatty acid oxidation enzymes. PPAR α is has been shown to have high expression rates in heart, adipose, and liver. PPAR γ is believed to be involved in adipocyte differentiation. PPAR γ is expressed in high levels in adipocyte tissues. PPAR δ (NUC1) is believed to be involved in a family of DNA binding proteins that are involved in adipogenesis and may be involved in early development. PPAR δ has been has been shown to have high expression in heart, kidney, and lung.

PPAR α is involved in the metabolic control of the expression of genes encoding fatty acid oxidation enzymes. Data from several experimental strategies have supported the hypothesis of the mechanism of action of PPAR α : 1) PPAR α is necessary for the induction of peroxisomal biogenesis in response to peroxisomal proliferating agents; 2) the target genes of PPARs are enzymes involved in cellular fatty acid oxidation which include mitochondrial, peroxisomal, and cytochrome P450 pathways; 3) PPAR α is activated by fatty acids or inhibitors of mitochondrial long-chain fatty acid import. It has been shown that PPAR α modulates the expression of genes encoding lipid metabolism enzymes, lipid transporters, or apolipoproteins. In an animal model of hyperlipidemia, activators of PPAR α was shown to decrease the lipid production in hepatocytes, however PPAR α activation also demonstrated tumor promotion within the same animals. Ligands that can specifically activate the lipostat enzymes while not turning on tumor production would be advantageous.

PPAR γ is thought to be involved in the differentiation of preadipocytes to adipocytes. Overexpression of PPAR γ in a non-adipose cell, i.e. nonadipogenic fibroblasts, results in the conversion to fat-laden adipocyte-like cells after exposure to a PPAR γ ligand. Another transcription factor family involved in adipogenesis is the CAAT/enhance binding protein, CEBP. CEBP α is expressed in high abundance in adipose tissue and may play a direct role in establishing and maintaining the fully differentiated adipocyte phenotype. This hypothesis is based mainly on the data that indicates CEBP α is expressed late in adipogenesis and after key enzymes are induced. In other studies it has been shown that PPAR γ and CEBP α expression can both be induced by CEBP β and CEBP δ . PPAR γ and CEBP α both induce the

expression of each other as well as activate and maintain the adipocyte proliferative and growth differentiation program.

5 The PPAR γ gene has two transcription start sites and translation results in two distinct proteins PPAR γ 1 and PPAR γ 2. Both are highly expressed in adipose tissue. As in other nuclear hormone receptors, PPAR γ is dependent on ligand activation. Currently, known biological ligands are 15-deoxy- $\Delta^{12,14}$ prostaglandin J, other prostanoids, and products from the linoleic acid pathway, i.e. oxLDL, HETE, 13-HODE and 9-HODE. Xenobiotics from the thiazolidinedione group, i.e. troglitazone, ciglitazone, and pioglitazone can directly activate PPAR γ .

10 Modulation of PPR activities are thought to be effective strategies for the development of products for therapy of cancers (breast, prostate, and acute promyleocytic leukemia), metabolic diseases including thyroid disease and diabetes mellitus. PPAR γ is expressed at significant levels in human primary and metastatic breast adenocarcinomas. Experimental evidence has suggested that the PPAR γ transcriptional pathway can induce terminal differentiation of malignant breast epithelial cells. Ligands known to activate PPAR γ have been shown to cause lipid accumulation, reduction of growth rate, and a reversion to a differentiated, less malignant state in studies of cultured breast cancer cells. Further, inhibition of MAP kinase, a negative regulator of PPAR γ , enhances the activation by a PPAR γ ligand (i.e. thiazolidinedione) sensitivity.

20 In studies of an animal model of diabetes, ligands that specifically activate PPAR γ (i.e. troglitazone), normalization of elevated glucose levels in obese animals was demonstrated. Studies have been conducted to ascertain the efficacy of thiazolidinediones to treat NIDDM. One product troglitazone (Rizulin) has achieved approval for human therapeutic use in the U.S.

25

In a recent study, it was determined whether genetic variation in the PPAR γ coding region was associated with obesity and insulin sensitivity or resistance, as well as type II diabetes mellitus (Deeb et al., Nature Genetics, 1998). It was determined that there was a single polynucleotide base substitution (C/G) which lead
5 to a substitution in the coding sequence of proline to alanine at amino acid position 12 (Pro12Ala). The study included two human populations, Finns and Japanese-Americans. It was determined that the relative frequency of the the alanine allele frequency in the Finn study population (nondiabetic, including some with impaired glucose tolerance) was 0.12 whereas the Japanese-American frequency was 0.022 in
10 type II DM patients, 0.039 in patients with impaired glucose tolerance, and 0.093 in normal subjects. In both populations there was an association of the Ala allele frequency and lower fasting insulin levels and body mass index, as well as higher insulin sensitivity; in the Finn population the values achieved statistical significance.

The study further demonstrated a functional correlation of the population
15 data with in vitro PPAR γ transcription factor binding affinities. In these experiments, it was shown that the Ala-isoform demonstrated a two- to five-fold decrease in relative affinity for the identified peroxisome proliferator response element, as well as a 36% faster off rate in comparison with the values detected for the PPAR γ Pro isoform. Confirmatory data in the form of reduced detectable
20 transactivation by the PPAR γ ligand in the case of the PPAR γ Ala isoform.

In addition, there is data to suggest that PPAR γ mRNA expression levels are reduced in obese individuals and that the the ratio of mRNA encoding PPAR γ is positively correlated with body mass index.

These data suggest that there is an association of reduced transcription
25 activation by the Ala PPAR γ allelic variant. Further suggesting, that there is a molecular mechanism for the observed body mass index and insulin sensitivity in the individuals having these allele polymorphisms. The data reported suggests that via reduced transcription of target genes that are involved in regulation of glucose homeostasis.

Example 28

Sulfonylurea receptor silent polymorphism and insulin levels

In a sub-population that is approximately three times more likely to acquire
35 type II DM, Mexican-Americans have higher insulin concentrations, and are more likely to exhibit insulin resistance. It has further been determined that in this population of Americans, hypeinsulinemia is a risk factor for the development of type II DM.

The high affinity sulfonylurea receptor (SUR1) is known to be involved in the regulation of insulin secretion. This receptor may be involved in type II DM. The SUR1 gene product is a functional part of the pancreatic β -cell KATP ion channel. The channel complex is composed of a two subunits, the sulfonylurea binding domain and the b-cell KATP channel responsible for conducting an inward rectifying potassium current. With the β -cell, metabolism of glucose produces changes in the relative concentrations of ADP and ATP which leads to a reduction of the KATP channel activation, causing a depolarization of the β -cell membrane and exocytosis of insulin. Within the nucleotide-binding fold region (NBF) of the SUR1, mutations have been shown to be autosomal recessive and lead to clinical familial hyper insulinemia. Other mutations in the SUR1 have been associated with Beckwith-Waldemann-syndrome associated malignant insulinomas.

In exon 31, there is a silent polymorphism (AGG/AGA) that encodes an arginine residue at position 1272. In the Mexican American study population that had the AGA genotype, there were higher fasting and 2 hr. insulin levels as well as a higher proinsulin to insulin ratio than those observed in the wild-type genotype subgroup. Between the two groups there were similar values for fasting glucose, body mass index, and waist circumference measurements.

Test Parameter	AGA	AGG	P value
Fasting insulin*	113.4	82.8	0.043
2 hr. insulin*	849.6	498.6	0.0003
Proinsulin/insulin ratio	0.068	0.056	0.030

*values in pmol/l

These data taken together suggests that there is an association between the SUR1 allelic variant and hyperinsulinemia in normal individuals from a high DM risk ethnic group.

Example 29

Vitamin D Receptor and Estrogen Receptor Polymorphisms and Response to Hormone Replacement Therapy

Bone mineral density (BMD), a predictor of risk of bone fractures, decreases rapidly in postmenopausal women. Hormone replacement therapy (estrogen) reduces the rate of or prevents the decrease in BMD. Genetic factors contribute to 60-80% of BMD variation. In a recent study (Deng et al., Hum Genet 103:576-585), it was shown that hormone receptor polymorphisms affect BMD in elderly women

and that genotype should be considered when prescribing hormone replacement therapy (HRT) to preserve bone mass in elderly Caucasian women.

A population of 108 women participated in the study. They were genotyped for polymorphic differences in their vitamin D (VDR) and estrogen (ER) receptors. Using restriction endonuclease specific sites within these genes, it was determined that the VDR has a polymorphic *BsmI* site (B or b) and the ER has two polymorphic sites, *XbaI* (X or x) and *PvuII* (P or p). In the placebo and HRT groups, the VDR and ER genotype groups had significant affect on the BMD measurements. An analysis of the gene-by-gene interaction revealed that the level of significance was reduced. The amount of variation in BMD attributable to the VDR and ER polymorphisms varied from approximately 1% (for the total body bone mineral content changes in the placebo or HRT groups) to approximately 18.7% (for the spine bone mineral density changes occurring in the HRT group). Significant genotype effects were observed in the xx, PP, or bb groups having a larger decrease of bone mass during the study period, whereas a genotype of XX, pp, or BB is associated with smaller decreases (or larger increase) of bone mass.

This study demonstrates and interaction of drug response with genotype with age/reproductive status.

Example 30

Cholesterol ethyl-transferase (CETP)

A well studied polymorphism in the first intron of the gene encoding cholesterol ester transfer protein (CETP) provides an example of a polymorphism in the non-coding region of a gene that has with an impact on drug efficacy via a recessive genetic mechanism.

The high-density lipoprotein (HDL) cholesterol concentration is inversely related to the risk of coronary artery disease. CETP has a central role in the metabolism of HDL and may therefore alter the susceptibility to atherosclerosis. The DNA of 807 men with angiographically documented coronary atherosclerosis was analyzed for the presence of a polymorphism in the gene coding for CETP. The presence of a DNA variation in a *Taq I* restriction enzyme site was referred to as B1, and its absence as B2. All patients participated in a cholesterol-lowering trial of the drug pravastatin designed to reduce cholesterol synthesis by inhibiting HMGCoA Reductase, and thereby arrest progression of, or induce the regression of coronary atherosclerosis and were randomly assigned to treatment with either pravastatin or placebo for two years. The B1 variant of the CETP gene was associated with both higher plasma CETP concentrations (mean [\pm SD], 2.29 ± 0.62 μ g per milliliter for the B1B1 genotype vs. 1.76 ± 0.51 μ g per milliliter for the B2B2 genotype) and lower

HDL cholesterol concentrations (34 ± 8 vs. 39 ± 10 mg per deciliter). In addition, a significant dose-dependent association between CETP genotype and the progression of coronary atherosclerosis in the placebo group (decrease in mean luminal diameter: 0.14 ± 0.21 mm for the B1B1 genotype, 0.10 ± 0.20 mm for the B1B2 genotype, and 0.05 ± 0.22 mm for the B2B2 genotype). This association was abolished by pravastatin. Pravastatin therapy slowed the progression of coronary atherosclerosis in B1B1 carriers but not in B2B2 carriers (representing 16 percent of the patients taking pravastatin). There was a significant interaction between pravastatin treatment and decreases in the mean luminal diameter ($P = 0.01$) and the minimal luminal diameter ($P = 0.05$). The association of the B1 allele with greater progression of diffuse atherosclerosis (i.e., greater decreases in the mean luminal diameter), as observed in the placebo group, was influenced by the use of pravastatin. In fact, the B1 allele appeared to be associated with less progression in the patients who were receiving pravastatin.

There was a co-dominant relation between the B1 allele and the efficacy of pravastatin in retarding the progression of coronary atherosclerosis. Carriers of two B1 alleles benefited most from treatment with pravastatin: they had significantly less progression of coronary atherosclerosis, as evidenced by smaller decreases in both the mean luminal diameter ($P = 0.001$) and the minimal luminal diameter ($P = 0.002$), than their B1B1 counterparts in the placebo group. Furthermore, carriers of only one B1 allele (B1B2) who were receiving pravastatin had significantly less focal atherosclerosis ($P = 0.01$) than their counterparts in the placebo group. Finally, B2B2 homozygotes had a nonsignificantly greater progression at the end of the study than their counterparts in the placebo group.

Both the association of the CETP TaqIB genotype with the decrease in either the mean luminal diameter or the minimal luminal diameter in the placebo group and the interaction between the genotype and pravastatin treatment remained significant after adjustments were made for the mean luminal diameter (or minimal luminal diameter) at base line, the base-line HDL cholesterol concentration, changes in HDL cholesterol concentrations, and activities of both hepatic lipase and lipoprotein lipase. The precise molecular mechanism that underlies the relation between the CETP gene variant and the angiographic response to pravastatin treatment cannot be deduced from this study. However, it may be related to plasma concentrations of CETP.

The observations suggest that high CETP concentrations, and therefore high levels of CETP activity, result in an enhanced transfer of cholesteryl esters to atherogenic lipoproteins and have negative effects on the structure and function of

the HDL pool, which increases the risk of coronary artery disease. This inference is in agreement with the observation that the pravastatin-induced reduction in CETP concentrations was associated with beneficial angiographic effects in patients who had high CETP concentrations -- that is, those who were homozygous for the B1 allele. In contrast, the reduction in CETP concentrations induced by pravastatin in patients with genetically determined low plasma concentrations of CETP -- that is, those who were homozygous for the B2 allele -- was associated with a lack of retardation of the progression of coronary atherosclerosis. On the basis of these results and the finding of an increased risk of coronary artery disease in subjects who are heterozygous for CETP deficiency, it is believed that a critical concentration of CETP is required for normal reverse cholesterol transport. In contrast, high plasma concentrations of CETP, as seen in placebo-treated B1B1 patients, may promote atherosclerosis by increasing the cholesterol component of atherogenic lipoproteins.

One skilled in the art can apply the knowledge of the CETP allelic differences by applying the techniques as described in the detailed summary section. In this way, one could identify the known allelic differences as described above to identify other allelic differences within the CETP gene. One would then be able to utilize molecular biological techniques to provide a diagnostic test to identify the genotypic differences within a selected group of volunteers or patients. In this way, using the methods for designing and implementing a clinical study described in the detailed description, one could implement a clinical trial to further test the significance of allelic variances on the response to pravastatin, other statins, other cholesterol lowering drugs or other candidate drugs that are known to interact with or affect the CETP gene pathway.

Example 31

Angiotensin converting enzyme (ACE)

The ACE polymorphism provides an example of a variance in the non-coding region of a gene with an impact on drug efficacy.

Angiotensin-converting enzyme (ACE) inhibitors, initially developed as antihypertensives, have been shown to reduce mortality in trials of patients with both symptomatic and asymptomatic left ventricular dysfunction and after acute myocardial infarction. An insertion/deletion polymorphism, consisting of a 287-base pair Alu repeat sequence, in intron 16 of the ACE gene, has been shown to predict approximately half of the variance in serum ACE levels between individuals. Homozygotes for the deletion allele (DD) have serum ACE levels twice as high on average as those homozygous for the insertion allele (II), whereas heterozygous (ID)

have intermediate levels. It has been demonstrated that genotype continues to predict residual ACE activity even after acute ACE inhibition with enalapril (Todd et al. Br J Clin Pharmacol 1995; 39:131-4). In a typical pharmacogenetic phase I design, comparing two groups of homozygotes healthy males, DD (n=12) and II (n=11) after genotyping 200 healthy normotensive men, the effect of enalapril, an ACE inhibitor drug, was significantly greater and lasted longer in the men homozygous for the II ACE genotype (Ueda et al. Circulation 1998; 98:2148-2153).

Example 32

Glycoprotein Integrin beta-3 subunit and Glycoprotein Integrin alpha-2 subunit (GPIIIa/GPIIb)

Glycoproteins IIIa (GPIIIa) and IIb (GPIIb) form the GPIIIa/GPIIb complex that belongs to a class of multisubunit integrin receptors that bind cell adhesion molecules. These receptors are composed of alpha and beta subunits referred to as GPIIb and GPIIIa, respectively. Together the GPIIIa beta and GPIIb alpha subunits form part of the platelet complex receptor, fibronectin receptor, and vitronectin receptor, and play a role in clotting.

The GPIIIa gene encodes a 788 amino acid polypeptide with a 26 residue signal peptide, a 29 residue transmembrane domain near the carboxyterminus and four cysteine rich domains of 33-38 residues each. (Zymrin et al., *J. Clin. Invest.* 81:1470-1475 (1988)). Two different antigenic forms of GPIIIa, alloantigens PlA1 and PlA2 (Platelet Antigen 1 and 2) have been described and can be distinguished using a monoclonal antibody. The most common form of GPIIIa, PlA1, is carried by 98% of the Caucasian population. The rarer form of GPIIIa, PlA2, carries a point mutation or single nucleotide polymorphism at base 192, changing a codon from CTG to CCG thereby causing a leucine to proline substitution at amino acid position 33 (Newman et al., *J. Clin. Invest.* 83:1778-1781 (1989)).

The GPIIb polypeptide is the larger component of the GPIIIa/GPIIb complex and includes two disulfide-linked subunits of 137 amino acids and 871 amino acids respectively. Two antigenic forms of GPIIb, Bak^a and Bak^b, have been described and can be distinguished using specific antisera. The rarer form of GPIIb, Bak^b, has been shown to have a T to G point mutation that results in an isoleucine to serine substitution at amino acid position 843 (Lyman et al., *Blood* 75:2343-2348 (1990)).

The presence of the C-nucleotide at position 192 of GPIIIa DNA can be readily detected by PCR amplification of a region bracketing position 192, followed by MspI digestion of the amplification products, as the C-substitution at that site creates a new MspI restriction site. Alternatively, the sequence at the variance site can be determined using sequencing of the amplification products to identify the nucleotide at the specified position.

The variant GPIIb forms can be detected using similar techniques as for GPIIIa variants by determining the nucleotide at position 2622 (corresponding to amino acid position 843).

It was found that each of the rarer variant sequences described above for GPIIIa and GPIIb correlated with the development of Alzheimer's disease, both separately and together. The variant GPIIIa and GPIIb alleles were found in Alzheimer's patients with an odds ratio of 1.82 and 1.45 respectively as compared to the wild-type alleles. Further, the two variant alleles were found to occur together in Alzheimer's patients as compared to normal subjects with an odds ratio of 3.74.

GPIIIa and GPIIb thus provide examples of variant sequences which result in amino acid substitutions in encoded polypeptides, where the variant sequences are correlated with the development of a disease or condition.

Similarly, other sequence variances in GPIIIa and GPIIb can be analyzed. In GPIIIa, these include for example, arg62term, leu117trp, asp119tyr, ser162leu, arg214gln, arg214trp, cys374tyr, tro407ala, arg636cys, and ser752tro. For GPIIb, the additional variance include leu183tro, gly242asp, the289ser, glu324lys, erg327his, gly418asp, arg553trm, ile565thr, gln747trp, and ser870term. The possible correlation of these variances with the development of cardiovascular disease can also be determined as for the previously identified variances.

Example 33

β 2-adrenergic Receptor Polymorphisms and Affects on Outcomes of Congestive Heart Failure

Several variances have been identified in the gene encoding β -adrenergic receptor. Some of the variances have been shown to affect receptor physiology, and may account, in part, for interpatient variation in the development, progression, and treatment outcomes of congestive heart failure. In a recent study, β -adrenergic receptor polymorphisms were correlated with clinical course of congestive heart failure (CHF) patients. Three amino acid polymorphisms identified in the β -adrenergic receptor were used to stratify patients diagnosed with CHF: Gln27Glu (Glu27 is associated with reduced receptor down-regulation), Arg16Gly (Gly16 is associated with increased down-regulation), and Thr164Ile (Ile 164 is associated with decreased coupling of the receptor with its GTP-binding protein). The allele frequencies of these polymorphisms were similar in normal and CHF patients, suggesting that the polymorphisms are not important in the etiology of CHF.

In a comparison of patients with the 164Ile variance versus the 164Thr variance (more common allele), the investigators determined that survival was greater for the 164Thr variance group over the study period; unadjusted relative risk

was 4.81 as compared to 3.69. The follow-up survival for individuals with the 164Ile genotype was 42% as compared with 76% for the 164Thr individuals. Although at the time of enrollment the two groups had similar clinical symptoms and other characteristics, there appeared to have been speedier decline in the patients with the Ile164 genotype. An analysis of the other two polymorphic sites (positions 16 and 27), revealed no detectable difference. These data taken together suggest that certain polymorphisms in pharmacologically and/or physiologically relevant proteins may influence the course of disease progression, and establishes the importance of determining genotypic differences to be able to identify individuals with specific genotypes in which earlier aggressive therapy would be warranted.

Example 34

Anthracycline Antibiotics

I. Description of Anthracycline Antibiotics

The anthracyclines are among the most important cancer drugs due to their broad effectiveness against various carcinomas, sarcomas, leukemias and lymphomas. The anthracycline antibiotics, daunorubicin and doxorubicin, were initially isolated from *Streptomyces peucetius* and have been in clinical use for decades. As a result of the effectiveness of these compounds hundreds of analogs have been produced synthetically or isolated from various microorganisms, including the recently developed compound idarubicin. Other recently isolated anthracyclines include DA-125, moflomycin, SM-5887, IT-62-B, WP631, KRN8602, AD198 and MX2 (all of which show antitumor activity), as well as 3'-O-demethyl mutactimycin, 4-O,3'-O-didemethyl mutactimycin and nothramicin (isolated from non-*Streptomyces* species). Many other compounds are known to those skilled in the art. These compounds can intercalate into DNA, and interfere with DNA replication and RNA transcription by steric action and by interfering with topoisomerase II function. The anthracyclines are associated with single- and double-stranded DNA strand scission, as well as production of radicals including superoxide, which induce damage to cellular components, including indirect DNA and protein alkylation. Free radical generation is dependent on cellular cytochrome p450 and quinone or hydroxyquinone moieties on adjacent rings in the anthracene backbone. Anthracyclines also bind membranes and alter membrane fluidity and transport, perhaps by radical formation. The anthracyclines are metabolized via hepatic oxidation to polyalcohols, with subsequent deglycosylation, formation of glucuronides and excretion into both bile and urine.

II. Current Indications for Anthracycline Antibiotics and Derivatives

Anthracycline antibiotics and derivatives are currently used to treat a broad spectrum of neoplastic diseases including, leukemias, lymphomas, sarcomas, neuroblastomas and cancers of the breast, thyroid, lung, stomach, and urogenital tract (endometrium, ovary, testicle). The synthetic, less cardiotoxic anthracycline derivative, mitoxantrone is indicated for acute nonlymphocytic leukemia (ANLL), and is also active against non-Hodgkins lymphomas and breast cancer.

III. *Limitations of Current Therapies Utilizing Anthracycline Derivative Antibiotics*

The clinical use of anthracycline derivatives is circumscribed by dose-limiting neutropenia and mucositis, and by cardiac toxicity, including an acute syndrome characterized by conduction and rhythm abnormalities or pump failure, and a chronic syndrome of cardiomyopathy that can lead to congestive heart failure. Anthracyclines are administered intravenously on various schedules. In the past dosing was by iv bolus every 3 or 4 weeks, but it has come to be appreciated that repeated small doses or continuous iv infusion is safer, especially in terms of cardiac toxicity, with no evident loss of efficacy. A major limitation of this family of compounds is that a cumulative dose in excess of 550 mg/square meter puts patients at risk of cardiomyopathy and resulting congestive heart failure. In the range of 1 to 10% of patients receiving a cumulative dose of at least 550 mg/square meter develop cardiomyopathy. Cardiomyopathy develops in a smaller fraction of patients receiving lower cumulative doses. All clinically tested anthracyclines are effective against some lymphomas and leukemias. Doxorubicin is also effective against certain solid tumors, such as those of the breast and lung, and a wide range of sarcomas. Doxorubicin is the drug of choice for the treatment of metastatic thyroid tumors. It is known to produce severe local toxicity to previously irradiated tissues, even when the two therapies are not administered contemporaneously. Although mitoxantrone treatment produces less nausea, vomiting, and alopecia than doxorubicin, acute myelosuppression and mucositis are frequently observed.

IV. *Impact of Genotyping on Drug Development for Anthracyclines*

The effectiveness of the anthracycline class of chemotherapeutics is believed to be related to its ability to cause DNA damage, either by direct free-radical damage or through the disruption of topoisomerase II function. Other effects of free radicals, which attack a wide range of important biological targets, are also likely to be important. Resistance to treatment can occur through several mechanisms, some of which are well studied. For example, (1) decreased levels of Topoisomerase II are frequently observed in anthracycline resistant cells. Levels of Topoisomerase II

(including TOP2 alpha and TOP2 beta genes) could be influenced by sequence variation or (in cancer tissue) by loss of heterozygosity, affecting interpatient variation in response or toxicity. (2) Topoisomerase III and Topoisomerase III beta levels or function may modulate response to anthracyclines. Anthracycline resistance in experimental systems is often mediated by drug efflux proteins, including the multidrug resistance transporter MDR1 and the multidrug resistance associated protein 1, as well as possibly other members of the ATP-binding cassette family (MRPs 1 through 6). (3) Variation in levels or function of phase I oxidative metabolism, glutathione-S-transferase and peroxidase, lung resistance related protein (LRP), breast cancer resistance protein (BCRP), and topoisomerase II. As anthracycline action is exerted through DNA damage, enzymes involved in the detection and repair of DNA damage (such as members of the xeroderma pigmentosum complementation groups (XP), the excision repair cross-complementation groups (ERCC), p53, the ataxia telangiectasia pathway) could also affect efficacy and toxicity. Polymorphisms in any of these gene pathways that affect the enzymatic activity of a gene product, the amount of a gene product, or the interaction of a gene product with anthracycline derivatives would be expected to affect either the initial response to treatment or systemic toxicity. There is also evidence that anthracyclines are probably less effective in MSI tumors; resistance attributable to impaired ability to detect DNA damage and thence activate apoptosis, and to increased mutation rate.

Impairment of essential free fatty acid metabolism is believed to play a role in therapeutic effect, as well as cardiac toxicity since administration of L-carnitine has been shown to partially reverse cardiac toxicity. The levels of iron, which serves as a mediator of free-radical damage, are also an important factor in cardiac toxicity, since treatment with the iron chelator, ADR-529 is protective. The levels of enzymes controlling oxidative stress, such as superoxide dismutase, are also known to be important determinants of anthracycline toxicity. Doxorubicin and its metabolite doxorubicinol are known to inhibit the action of ion pumps known to be involved in cardiac muscle contraction such as the sarcoplasmic reticulum calcium-dependent ATPase, SERCA1.

Polymorphisms gene products involved in fatty acid metabolism, iron metabolism, calcium concentration, and free radical quenching that alter total enzymatic activity would all be expected to be predictive of toxicity, particularly if the polymorphism is in a gene product whose expression is restricted to or enriched in cardiac tissue (i.e. SERCA1). As an extension, any polymorphism correlated with reduced cardiac function, either manifest or occult, might predispose patients receiving anthracycline antibiotics or derivatives to cardiac toxicity.

Example 35

Antimicrotubule Agents

I. Description of Vinca and Taxus Alkaloids and Derivatives

5 The vinca alkaloids, originally extracted from the periwinkle, *Vinca rosea*, and the taxus alkaloid, taxol, isolated from the Western yew, *Taxus brevifolia*, exert their pharmaceutical effects by promoting the destabilization or polymerization, respectively, of microtubule structures involved in cell architecture and division. The vinca alkaloids, and vinorelbine, a newer, better tolerated derivative, share a
10 heterodimeric, heterocyclic structure and bind tubulin with a 1:1 stoichiometry. Binding prevents mitotic spindle function and normal chromosome segregation, leading to apoptotic cell death. Colchicine, an alkaloid extracted from the autumn crocus, *Colchicum autumnale*, shares this mechanism of action, but its use is restricted to the treatment of gout.. Taxol, and its more potent derivative, docetaxel,
15 are complex terpenoid compounds that contains a taxane ring nucleus. Treatment with taxus alkaloids causes the accumulation of microtubule aggregates, leading to abnormal cell morphology and arrest of cell division during mitosis. Prior treatment with doxorubicin, which antagonizes cell cycle progression, can reduce therapeutic benefit and increase toxicity. Discodermolide, a polyhydroxylated alkatetraene
20 lactone, binds tubulin at the same location as taxol, causing tubule aggregation in an analogous manner. Epothilone A and B, isolated from the myxobacterium *Sorangium cellulosum*, and desoxyepothilone B, a less toxic derivative, are also known to exert their antiproliferative effects through microtubule stabilization. Rhizoxin, combretastatin A4, and amphethinile are other recently identified natural
25 product microtubule inhibitors.

II. Current Indications for Antimicrotubule Agents

 The vinca alkaloids differ significantly in their antitumor effects as well as actions on normal tissues. Vincristine is a standard component of regimens for
30 treating pediatric leukemias and solid tumors and is frequently used to treat adult lymphomas. Vinblastine is utilized primarily for the treatment of lymphomas, neuroblastoma, breast and choriocarcinomas, and as a second-line therapy for various solid tumors. The most important use of vinblastine is conjunction with bleomycin and cisplatin in the curative therapy of testicular cancer. Vinorelbine
35 has been successfully used as a monotherapy to treat non-small cell lung cancer and breast cancer. Treatment is via weekly intravenous infusion until dose-limiting toxicity is observed or triweekly during vinblastine treatment of testicular cancer.

III. *Limitations of Current Therapies Utilizing Antimicrotubule Agents*

Vinblastine and vinorelbine cause leukopenia and vincristine can cause hypertension through inappropriate vasopressin secretion. Alopecia occurs in approximately 20% of patients receiving vincristine, but is reversible, often without
5 cessation of treatment. All three vinca alkaloids can cause neurotoxicity, but vincristine has predictable cumulative effects. Neurotoxic symptoms include numbness and tingling of the extremities, loss of deep tendon reflexes, and muscle weakness, the latter prompting suspension or reduction of dosing.

Neutropenia and mucositis are frequently observed during taxol treatment, with peripheral stocking-glove sensory neuropathy seen as the dose-limiting
10 toxicity. Many patients experience myalgia for several days after dosing. Dosing can be via short (1-6 hour) or long (72-96 hour) infusions. Pretreatment with corticosteroids or antihistamines has been used to avert hypersensitivity reactions seen with shorter dosing schedules and mucositis is a frequent complication of
15 longer schedules.

Paclitaxel and docetaxel undergo oxidative hepatic metabolism via CYP2C8 and 3A4 and are particularly toxic in patients with reduced liver function.

IV. *Impact of Genotyping on Drug Development for Antimicrotubule Agents*

The effectiveness of antitubule agents is related to their ability to prevent mitosis by affecting spindle assembly and disassembly, by preventing secretory vesicle translocation, and by perturbing normal cellular architecture. Resistance to treatment can occur through alterations in microtubule-associated protein 4 (MAP4),
20 beta tubulin (TUBB), multidrug resistance transporter (MDR1), Bcl-X/Bcl-2 binding protein (BAD), and tyrosine kinase type receptor HER2/NEU. Polymorphisms in
25 any of these gene pathways that affect the enzymatic activity of gene product, amount of gene product, or interaction between gene product and antimicrotubule agent would be expected to affect initial response to treatment.

Since the vinca and taxol classes of antimicrotubule agents have opposing
30 effects on microtubule polymerization state, resistance to one class of agents is often associated with collateral sensitization to the other. Analogously, tubulin or MAP4 polymorphisms that stabilize microtubules would be expected to respond better to taxol therapy than to vinca alkaloid therapy. Microtubules are composed of alpha and beta tubulin subunits and each is encoded by a 15-20 member, dispersed,
35 pseudogene-containing, multigene family restricted in expression to a subset of tissues. For instance, alpha-1 and beta-2 tubulins are restricted to the testis. Polymorphisms in these subunits would be expected to affect primarily the efficacy of antimicrotubule agents for the treatment of testicular cancers.

Taxol derivatives are metabolized primarily by cytochrome P450s CYP2C8 and 3A4. Polymorphisms that affect the enzymatic activity or amount of these gene products would be expected to be predictive of toxicity, especially hepatic and neural. Alpha-3, beta-4, and beta-5 tubulin subunits are restricted to differentiated neural tissues and polymorphisms in these genes affecting protein levels or microtubule agent binding might be predictive of neural toxicity.

Example 36

Topoisomerase Inhibitors

I. *Description of Topoisomerase Inhibitors*

Etoposide and teniposide are two semisynthetic glycoside derivatives of podophyllotoxin, a toxic alkaloid from the mayapple, *Podophyllum peltatum*. These compounds have a similar spectrum of antitumor activity and exert their cytotoxic effects by their interaction with cellular topoisomerase II, an enzyme required during DNA replication. The complex between DNA topoisomerase II and etoposide or teniposide is capable of double stranded DNA strand scission, but not strand exchange or ligation. The resulting DNA damage initiates apoptotic cell death. The bulk of administered etoposide is excreted via the kidney unchanged whereas approximately 80% of teniposide is recovered from urine as metabolites. Amsacrine, 4-(9-acridinylamino)-N-(methanesulfonyl)-m-anisidine, is an additional inhibitor of DNA topoisomerase II in clinical trials as part of multiagent induction chemotherapeutic regimen for acute myelogenic leukemias.

Topotecan and irinotecan, derivatives of camptothecin, originally isolated from the bark of *Camptotheca acuminata*, bind DNA topoisomerase I and cause DNA fragmentation and apoptotic cell death in a manner entirely analogous to the podophyllotoxins. Topotecan is also oxidized by liver cytochromes prior to being excreted via the kidneys. Irinotecan is a prodrug and requires activation by a carboxylesterase to its active metabolite, SN-38. Elimination after hepatic oxidation is via biliary excretion.

II. *Current Indications for Topoisomerase Inhibitors*

Etoposide and teniposide are active against a broad spectrum of tumor types including testicular, small cell lung, various lymphomas, acute granulocytic leukemia, and Kaposi's sarcoma. When combined with cisplatin and bleomycin for testicular tumors and with cisplatin for small cell lung carcinomas, these compounds become the treatment of choice. Administration can be achieved orally (etoposide), but the preferred route is intravenous, with dosing repeated at 2 to 3 day intervals.

Teniposide is better tolerated in patients with compromised renal function than is etoposide.

Topotecan is used primarily for the treatment of ovarian and small cell lung carcinomas and is administered via daily intravenous infusion for 3 or more days.

5 Irinotecan is indicated for the treatment of colorectal cancer and is administered by slow intravenous infusion once weekly for 4 weeks, followed by a two week recovery period. This dosing cycle is repeated until the desired therapeutic endpoint is reached.

10 III. *Limitations of Current Therapies Utilizing Topoisomerase Inhibitors*

The dose-limiting toxicity for etoposide is leukopenia which peaks approximately two weeks after the onset of treatment. Nausea, vomiting, stomatitis, and diarrhea occur in about 15% of patients receiving etoposide intravenously and 55% who receive it orally. Hepatic toxicity, phlebitis, dermatitis, and reversible
15 alopecia are also observed. Etoposide treatment of childhood acute lymphoblastic leukemia (ALL) has been linked with a secondary myeloid/lymphoid or mixed-lineage leukemia involving a translocation event at 11q23, a region involved in pluripotent stem cell differentiation, that appears 1 to 3 years subsequent to therapy. Teniposide is also used for the treatment of refractory ALL and is associated with
20 myelosuppression, nausea, and vomiting. Undesired effects of topotecan and irinotecan treatment are similar to those of topoisomerase II inhibitors. Nausea associated with irinotecan is often severe enough to require treatment.

25 IV. *Impact of Genotyping on Drug Development for Topoisomerase Inhibitors*

Resistance to topoisomerase I and II inhibitor therapy can be caused by alterations in topoisomerase activity, topoisomerase levels, or in inhibitor accumulation (MDR1). Multiple amino acid polymorphisms have been reported for both topoisomerases (Table 3) that could potentially affect enzyme activity, drug binding, or protein levels. It has also been shown that cell lines lacking functional
30 Ku86, a protein involved in double-stranded DNA break repair, are hypersensitive to etoposide, suggesting that polymorphisms affecting the levels or activity of this protein in normal tissues or tumor might also be an important determinants of toxicity and efficacy, respectively.

A serious undesired outcome of etoposide treatment of ALL is the
35 development of therapy-related, secondary nonlymphocytic leukemia. Studies have shown that even though etoposide is a known mutagen, mutation rates are not significantly enhanced during treatment, suggesting that patients that acquire secondary leukemia have a natural predisposition. The appearance of secondary

acute myelomonocytic or promyelocytic leukemia is related to DNA translocations involving the 11q23 region that contains the *Drosophila* trithorax homeobox transcription factor homolog MLL or the 15q22 region that contains the PML gene, whose product contains transcription factor consensus elements. The latter
5 translocation produces a hybrid protein containing the DNA binding portion of the PML protein fused to the hormone binding portion of the retinoic acid receptor alpha protein. The 11q23 region is known to contain folate-sensitive fragile site FRA11B, suggesting that polymorphisms in genes involved in folate metabolism may play a contributing role to the appearance of secondary leukemia.
10 Polymorphisms in genes involved in non-pathological DNA rearrangements such as immunoglobulin and T-cell receptor rearrangements (i.e. ataxia telangiectasia, DNA ligase, Ku86, Ku70, etc.), that alter the amount or activity of their gene product, represent candidate genes for association with susceptibility to etoposide treatment-related, secondary leukemia.

Example 37

Platinum Coordination Complexes

I. Description of Platinum Coordination Complexes

The cytotoxic nature of platinum compounds was first observed in *E. coli* in
20 1965 and traced to inorganic platinum adducts with ammonium and chloride ions. Of the thousands of platinum derivatives that have been synthesized and tested, cisplatin (cis-diaminodichloroplatinum II) and carboplatin (diaminocyclobutanedicarboxylatoplatinum II), have proven most valuable in the clinic. These platinum complexes seem to enter cells by diffusion and are activated
25 by hydrolysis to a hydrated, cationic diamino platinum II species believed to react with nucleic acids and proteins. The N7 position of guanine is particularly prone to modification and intrastrand and interstrand DNA cross-links between proximal guanine bases and adenine and guanine bases are formed. These adducts inhibit DNA replication and transcription, leading to apoptotic cell death. The bulk of
30 compound is excreted unchanged in the urine.

II. Current Indications for Platinum Coordination Complexes

Cisplatin produces good response in a broad range of cancers including those of the bladder, head and neck, endometrium, and small cell lung carcinoma. It has
35 been used alone, or in combination with paclitaxel, cyclophosphamide, or doxorubicin for the treatment of ovarian cancers and is curative in combination with bleomycin, etoposide, and vincristine in about 85% of testicular cancers. Platinum compounds are also used as sensitizers for radiation therapy. Administration is via

intravenous infusion subsequent to hydration with saline to minimize renal toxicity. Dosing regimens are 20 mg/m² for five consecutive days or 100 mg/m² given once every four weeks.

5 III. *Limitations of Current Therapies Utilizing Platinum Coordination Complexes*

Marked nausea and vomiting occur in almost all treated patients, but can be controlled with ondasteron or corticosteroids. Renal electrolyte wasting is a frequent occurrence and may lead to tetany and/or seizures. As a result, it is recommended that plasma magnesium levels in patients receiving platinum
10 compounds are routinely monitored. The most serious adverse effects of platinum coordination compound therapy are neurological. Tinnitus and hearing loss in the high frequency range become more frequent and severe with repeated doses and tend to be more pronounced in children. Cisplatin induced neuropathies were first recognized in the early 1980s. Early indications are reduced decreased vibratory
15 sensitivity in toes, loss of ankle jerks, and loss of sural nerve response. Peripheral nerves may show axonal degeneration and secondary myelin breakdown. Cisplatin-induced peripheral neuropathy may worsen after discontinuation of treatment, can linger for months to years after cessation of treatment, and can result in death.

20 IV. *Impact of Genotyping on Drug Development for Platinum Coordination Complexes*

Resistance to platinum compound therapy is generally acquired through the selection of mutant forms of the tumor suppressor protein p53. This protein is involved in the detection of DNA damage and DNA damage-related cell-cycle arrest
25 and apoptosis. Tissue culture studies have shown that these mutants appear to arise spontaneously and become enriched only after platinum treatment. Numerous polymorphisms in the p53 gene have been reported and any that reduce protein amounts or DNA binding activity would be expected to correlate with lower treatment efficacy. As the cytotoxicity of platinum coordination complexes are
30 directly related to their charge and ability to alkylate DNA, enzymes involved in the detection and repair of DNA damage (such as members of the xeroderma pigmentosum complementation groups (XP), the excision repair cross-complementation groups (ERCC), Ku86/70, etc.) could also affect efficacy and toxicity. Elevated levels of some of these enzymes has been found in platinum-
35 resistant ovarian tumor samples. Polymorphisms in any of these gene pathways that affect the enzymatic activity of gene product, the amount of gene product, or the interaction of gene product with platinum-induced DNA adducts would be expected to affect either the initial response to treatment or systemic toxicity.

Neural platinum toxicity appears to be mediated by free, inorganic platinum. Platinum accumulation is greatest in dorsal root ganglia and lowest in neural tissues protected by the blood-brain barrier, consistent with primarily peripheral toxicity. Several agents including glutathione, metallothionein, nerve growth factor,
5 neurotrophin 3, glutamate, and S-2-(3-aminopropylamino)-ethylphosphorothioic acid (WR 2721) have shown promise in animal models as a neuroprotectants.

Glutathione is synthesized from the amino acids cysteine, glutamate, and glycine by the consecutive action of gamma-glutamylcysteine synthetase and glutathione synthetase, encoded by single-copy genes and expressed ubiquitously.
10 Polymorphisms in the genes required for glutathione synthesis would be expected to affect primarily the efficacy of platinum compounds. In contrast, metallothioneins are encoded by a 10 to 12 member multigene family. Metallothionein 3 expression is restricted to neural tissue and polymorphisms could be associated with neural toxicity. Polymorphisms in these genes influencing protein levels or activity would
15 be expected to be important predictors of neural toxicity.

Example 38

Steroid Hormone Derivatives

20 I. *Description of Steroid Hormone Derivatives and Related Agents*

Steroidal agents include adrenocorticosteroids and analogs, agents such as aminoglutethimide that regulate the levels of adrenocorticotrophic hormone (ACTH), antiestrogens such as tamoxifen, progestins such as hydroxyprogesterone caproate and megestrol acetate, antiandrogens such as flutamide, and gonadotropin releasing
25 hormone (GNRH) and analogs such as goserelin and leuprolide, that decrease secretion of leutenizing hormone (LH) and follicle stimulating hormone (FSH) by the pituitary after long term administration. Depression of FSH and LH levels, in turn, decreases circulating levels of testosterone to castration levels in men and estrogen levels in women to postmenopausal.

30 Flutamide, tamoxifen, panomifene, and raloxifene are recently developed androgen and estrogen receptor modulators that block the activation of transcription required for the maintenance and function of hormone-responsive tissues. In the absence of androgen- or estrogen-stimulated transcription, proliferation of metastatic prostate and breast cancers is greatly reduced. These agents are usually used in
35 conjunction with cytotoxic chemotherapeutic agents such as alkylating agents, platinum compounds, anthracyclines, topoisomerase inhibitors, and microtubule polymerization/depolymerization modulators. Tamoxifen, cyclosporin A, and

verapamil, have all received great clinical attention due to their ability to reverse MDR1-associated drug resistance.

II. *Current Indications Steroid Hormone Derivatives and Related Agents*

5 Steroidal agents and agents that indirectly affect steroid levels are used against a rather limited number of neoplastic diseases. Corticosteroids such as dexamethasone and prednisone are used alone or in combination with vincristine and anthracyclines, with or without methotrexate and asparaginase, for the treatment of acute and undifferentiated lymphoblastic leukemia, due to their ability to block
10 lymphocyte proliferation. Aminoglutathimide treatment of metastatic breast cancer with concomitant hydrocortisone supplementation has been largely supplanted by tamoxifen, which acts directly to limit estrogen receptor signaling. The orally available aromatase inhibitors vorozole, letrozole, exemestane, formestane, and anastrozole are currently in development as second-line therapies for the treatment
15 of advanced breast cancer.

Tumors stemming from endocrine tissues and steroid-responsive tissues frequently retain steroid hormone responsiveness initially. This is true for tumors of breast, prostate, testicular, ovarian, and endometrial origin, as well as other less frequent cancers.

20 Localized prostate cancer is often curable with surgery and/or radiation therapy, but androgen-deprivation therapy becomes the primary hormonal treatment for metastatic disease. Treatment leads to a reduction in symptoms, but is considered palliative since tumors eventually become insensitive. Reduction in serum androgen can be achieved by bilateral orchiectomy, generally reserved for
25 older patients, GNRH analog treatment, and flutamide treatment alone or in conjunction with GNRH analogs. Flutamide decreases the original flare of prostate tumor growth as a result of transient LH increase in GNRH analog monotherapy. Leuprolide and goserelin are administered via intramuscular and subcutaneous injection and are released slowly into the bloodstream; both agents are also indicated
30 for the treatment of breast and endometrial cancers. Flutamide is administered orally, generally three times daily and is currently approved only for use in combination therapy.

Tamoxifen has replaced diethylstilbesterol as the hormonal treatment of choice for estrogen receptor-bearing breast cancers. Both tamoxifen and raloxifene
35 have found recent application for the prevention of postmenopausal decreases in bone density. Tamoxifen is administered by mouth twice daily and is often used for prolonged periods in the context of adjuvant therapy following the initial treatment

of primary breast cancers. The drug is metabolized by oxidation and formation of glucuronides and excreted into the stool via bile.

III. *Limitations of Current Therapies Utilizing Steroid Hormone Derivatives and Related Agents*

As a class, the hormonal agents are extremely well tolerated. Leuprolide, goserelin and flutamide treatment can produce some of the symptoms of menopause including hot flashes, as well as a loss of libido and impotence, but none of these complications is dose limiting. Doses of tamoxifen 20-times the recommended dose are associated with retinal degeneration, but standard doses produce symptoms similar to menopause, weight gain, and gastrointestinal disturbances, none of which is dose limiting. The aromatase inhibitors produce similar side effects. Prolonged use of tamoxifen, such as during adjunct treatment, chemoprevention, or for prevention of postmenopausal osteoporosis, has been linked to the development of endometrial cancers. Patients receiving the standard dose of tamoxifen for two years are twice as likely to develop endometrial cancer than untreated controls.

IV. *Impact of Genotyping on Drug Development for Steroid Hormone Derivatives*

Antiestrogen therapy in the context of chemotherapy is generally indicated only for estrogen-receptor bearing tumors. Estrogen receptor polymorphisms that affect protein levels, DNA or estrogen binding, or interaction with other transcription factors would be expected to correlate with treatment outcome. More-specifically, decreases in any of these parameters should decrease efficacy. Expression of epidermal growth factor receptor (EGFR) and tyrosine kinase-type cell surface receptor HER2/NEU correlates with poor response to tamoxifen even in estrogen receptor positive tumors, but neither EGFR or HER2/NEU appear to be amplified during the course of treatment. As noted above, HER2/NEU expression also correlates with poor prognosis during treatment with antimicrotubule agents, suggesting that ectopic or enhanced expression of growth factor receptors can overcome the growth inhibition caused by cytotoxic agents.

Steroid hormone derivatives are metabolized via cytochrome P450 and flavin containing monooxygenases and by conjugation to sulfates and glucuronates for elimination. Oxidative metabolism of tamoxifen by liver microsomal fractions has been well characterized and involves the formation of 4-hydroxyl, 4'-hydroxyl, N-oxide, N-desmethyl, 3,4-dihydroxyl, and 3,4-epoxyl derivatives. The latter, reactive epoxide species is formed in large amounts in rats, but not mice or humans, and is thought to account for increased liver carcinogenesis in this species. Formation of the N-oxide is believed to be mediated by a flavin containing monooxygenase

(FMO), while other reactions appear to be carried out by cytochromes, especially CYP3A4 (N-demethylation) and 2D6 (4-hydroxylation). Polymorphisms in genes encoding FMO enzymes 1 and 3-5 (FMO2 is inactive), or CYP3A4 and 2D6, or sulfotransferases, or glycosyltransferases that affect protein amount or activity
5 would be expected to influence efficacy by increasing or decreasing elimination.

Polymorphisms in the gene(s) encoding the enzyme(s) responsible for 3,4-epoxide formation that affect protein amount or activity would be expected to correlate with the mutagenic effects of tamoxifen, especially with the occurrence of treatment-related endometrial cancers.

10

Example 39

Inhibitors of Signal Transduction

I. Description of Signal Transduction Inhibitors

Signal transduction is the processes whereby external cellular stimuli are
15 converted into changes in protein expression. The usual chain of events is (1) interaction of a ligand with a cell surface receptor, (2) ligand-induced changes in the three-dimensional structure of the receptor, including dimerization, that are transmitted to the cytoplasmic face of the plasma membrane, (3) transmission of these changes to transcription factors in a complex, multienzyme cascade that
20 generally involves a change in the phosphorylation state of enzymes in the cascade, modulating their activity or ability to interact with other proteins in the cascade, and (4) modulation of the availability or activity of gene specific transcription factors through changes in phosphorylation status, oligomeric state, cellular localization, synthesis, or degradation.

25 Changes in the signal transduction process play a pivotal role in the etiology of neoplastic transformation and disease. The enzymes involved are usually members of a closely-related, multienzyme family, that display complex temporal regulation during development and are differentially expressed in normal tissues. Recent advances in understanding the molecular biology of these pathways and
30 technical breakthroughs in both combinatorial chemistry and high-throughput screening have added novel, synthetic agents to the small number of known, naturally occurring signal transduction inhibitors.

Current signal transduction inhibitors affect phosphorylation and dephosphorylation steps associated with receptor and soluble kinases as well as
35 protein phosphatases. Many subtype selective and nonselective inhibitors of protein kinase C (PKC) were initially isolated from natural sources. These include the protein kinase C inhibitors staurosporin, herbimycin A, lavendustin A, and erbstatin, originally isolated from various *Streptomyces* species; the tyrosine

kinase inhibitors emodin, cytovaricin B, angelmicin B, geldanamycin, and genistein isolated from *Talaromyces*, *Streptomyces*, and *Lupinus* species; the phosphatidylinositol 3-kinase inhibitor wortmannin isolated from *Talaromyces flavus*; and the protein phosphatase inhibitor okadaic acid isolated from the black sponge, *Prorocentrum oncauum*. Erbstatins, which bind the ATP-binding site of PKC, also have activity against topoisomerases I and II. Numerous synthetic derivatives of these compounds that enhance stability and availability, as well as novel compounds, have been produced and assayed in biological systems more recently. These include the protein kinase C inhibitors L86-8275, H7, LY333531 (Eli Lilly), safinol (Sphinx/Eli Lilly) and CGP41251 (Ciba-Geigy); the tyrosine kinase inhibitors SU5416 (Sugen), specific for VEGF receptor-associated tyrosine kinase; ZM 252868, ZD1839 (Zeneca), PD153035 (Parke-Davis), and CGP 52411 (Ciba-Geigy), specific for EGF receptor-associated tyrosine kinase, CEP-701 (KT-5555) and K252a, specific for TRK-type receptor-associated tyrosine kinase, KN-62, specific for Ca^{++} /calmodulin-dependent protein kinase II; tyrosine kinase inhibitors of the tyrphostin class, as exemplified by AG1714 (4-nitrobenzylidene malononitrile); the phosphatidylinositol 3 kinase inhibitors of the 3-deoxy-D-myoinositol 1-phosphate/1-phosphonate class; the protein serine/threonine phosphatase inhibitor endothall; and the tyrosine phosphatase inhibitor bis(maltolato)oxovanadium(IV).

Bryostatin, a macrolactone originally isolated from marine sponges, inhibits signal transduction through an as yet unknown mechanism, but likely to involve PKC isozymes.

The growth factor 1 family of transmembrane receptors, including epidermal growth factor receptor (EGFR) and members of the ERB-B family, are overexpressed in a wide variety of solid tumors, particularly squamous cell carcinomas of the head and neck, lung, and cervix. The oncogene CBL, implicated in pre/pro B-cell lymphomas, and its cellular counterpart C-CBL, mediate the recycling/degradation of EGFR members. EGFR members are already important therapeutic targets and C-CBL represents an important future drug target.

Mutations in members of the RAS G protein superfamily are the most common initiators of neoplastic transformation, occurring in approximately 40% of colorectal cancers, 90% of pancreatic cancers, 30% of lung adenocarcinomas, and 25% of acute myeloid leukemias. Inhibitors of RAS farnesylation are currently in clinical trials.

RAS control of cell cycle decisions and of transcription factor phosphorylation by Janus kinase (JUNK) is mediated by at least four distinct signaling pathways including the mitogen-activated protein kinases (MAPKs) and

phosphatidyl inositol 3 kinases (PIK3s). Inhibitors designed to members of these multigene families are in early development, show great promise. Silymarin, a flavonoid antioxidant isolated from milk thistle, is a MAPK modulator and has shown great efficacy in the chemoprevention of skin cancer in a mouse model.

5

II. *Current Indications for Signal Transduction Inhibitors*

Many of the signal transduction inhibitors listed above show promising antineoplastic activity in tissue culture and animal models, but only a few compound are currently in early clinical development. The staurosporine derivative UCN-01 is being tested for activity in advanced or refractory solid tumors, lymphoproliferative disorders, and lymphoid malignancies and SU5416 is being tested in combination therapy with 5-fluorouracil and leucovorin for metastatic colorectal cancer. Bryostatin is in early clinical trials alone, or in combination with cisplatin and paclitaxel for refractory and advanced malignancies including unresectable stomach, esophagus, anus, prostate, or non-small cell lung cancer. It is anticipated that upon further development, members of this class of agents will be indicated for the treatment of a broad range of neoplastic diseases. The phosphatidylinositol 3 kinase inhibitor, wortmannin, has been shown to be active as a radiosensitizer *in vitro*, suggesting potential utility in the radiation therapy of tumors.

20

III. *Impact of Genotyping on Drug Development for Signal Transduction Inhibitors*

Activation of the MAPK pathway has been shown to correlate with poor prognosis for prostate cancers as well as resistance to androgen ablation therapy. In both colorectal and breast tumors, expression in malignant tissue was elevated while expression in surrounding tissues was normal. The oncogenic potential of MAPKs has been demonstrated in a mouse model, where a lysine to glutamate mutation appears to cause cellular transformation. These findings all highlight the important role of the MAPK pathway in the initiation and progression neoplastic disease.

25

There is also evidence for the direct involvement of the PKC pathway in neoplastic disease: a point mutation at position 294 of alpha-protein kinase C, leading to an aspartic acid to glycine substitution, has been linked to pituitary tumor invasiveness.

30

Overexpression of EGFR has been strongly associated with the transition from superficial to invasive bladder cancers. Enhanced cellular motility is a prerequisite to invasion and can be inhibited in an *in vitro* model by wortmannin, a specific inhibitor of phosphatidylinositol 3 kinase, implicating this class of enzymes in bladder cancer progression. The structurally related ataxia telangiectasia gene product, when mutated, causes a predisposition to malignancy.

35

Polymorphisms in genes encoding receptors and proteins of the signal transduction pathway as detailed above and in Tables 1-3, or related proteins yet to be discovered, which influence protein amounts, activity, interaction with other proteins or drugs, would be expected to have prognostic value for risk assessment, treatment efficacy, and toxicity.

Example 40

Inhibitors of Cell Cycle Control

a) Description of Cell Cycle Control Inhibitors

The control of cell cycle progression and division is through a complex signaling pathway, such as described above, at the heart of which are the cell division cycle (CDC) proteins, CDC kinases (CDCKs), cyclins, cyclin-dependent kinases (CDKs), and cyclin-dependent kinase inhibitors. All exist as members of multigene families that show temporally regulated and tissue-specific expression. Ubiquitin ligases and the ubiquitinated protein proteolysis pathway are involved in modulating cyclin levels during the cell cycle.

Interest in this class of macromolecules as drug development targets was sparked by the observation that the level of various cyclin-dependent kinases and cyclin-dependent kinase inhibitors differed between normal tissues and a wide variety of tumor types and could be prognostic of treatment outcome. Low to absent levels of the cyclin-dependent kinase inhibitor 1B (p27, KIP1) has been shown to be predictive of unfavorable prognosis in a variety of tumors. Ectopic expression of KIP1 in human brain tumor cells has been shown to reverse some of the changes of neoplastic transformation. In contrast, elevated levels of the cyclin-dependent kinase inhibitor 2A (p16, INK4, MTS1), is associated with progression and unfavorable prognosis in prostate and ovarian cancers. This protein is also the target of frequent somatic mutation.

Several natural and synthetic inhibitors of CDK and CDCK function have been isolated. These include flavopiridol, butyrolactone I, and the purine derivatives aminopurvalanol, olomoucine, and roscovitine.

II. *Current Indications for Cell Cycle Control Inhibitors*

The CDK and CDCK inhibitors listed above have demonstrated efficacy in a number of transformed cell types in tissue culture, but only flavopiridol is advanced clinical development for refractory and recurrent colorectal cancer, adenocarcinoma of the prostate, lymphocytic leukemia, and non-Hodkin's and mantle cell

lymphomas, either as a monotherapy or in combination with taxol and cisplatin compounds. It is anticipated that upon further development, members of this class of agents will be indicated for the treatment of a broad range of neoplastic diseases and hyperproliferative disorders such as psoriasis and restenosis.

5

III. *Impact of Genotyping on Drug Development for Cell Cycle Control Inhibitors*

Expression of cyclin-dependent kinase inhibitor 1A (p21/WAF1) is induced by the tumor suppressor protein p53 in response to DNA damage, thereby playing a direct role in

10

mediating p53-induced G1 arrest. Two polymorphisms in the p21 gene, a serine to arginine change at codon 31 a C to T transition in non-coding sequence, show increased prevalence in prostate adenocarcinoma and squamous cell carcinoma of the head and neck. Similarly, low to absent levels of the cyclin-dependent kinase inhibitor, p27/KIP1 are associated with poor clinical outcome in gastric and

15

colorectal cancers. Cyclin D1 expression levels have also been shown to correlate with progression and prognosis in non-small cell lung cancers, estrogen receptor-positive breast cancers, esophageal cancer, and gastric cancers. However, the correlation can be positive or negative, depending upon cancer type, making it likely that cyclin D1 levels are not the directly responsible for neoplastic transformation in these tumors, and that they are a poor prognostic indicator for tumors in general. However, analysis of patients diagnosed with squamous cell carcinomas showed that G/G homozygotes of the silent G/A polymorphism in exon 4 of cyclin D1 tend to exhibit less differentiated tumors and have shorter remission times than G/A heterozygotes and A/A homozygotes. These findings carried over to various tumor subtypes, including laryngeal and pharyngeal.

20

25

Polymorphisms in genes encoding cell cycle checkpoint proteins, and proteins involved in cell cycle progress as detailed above and in Tables 1-3, or related proteins yet to be discovered, which influence protein amounts, activity, interaction with other proteins or drugs, would be expected to have prognostic value for risk assessment, treatment efficacy, and toxicity.

30

Example 41

Angiogenesis Inhibitors

35

i. Description of Angiogenesis Inhibitors

The utility of angiogenesis inhibitors for the treatment of solid tumors was first recognized by Folkman and colleagues in 1980. Angiogenesis, the creation of vasculature, is a process that insures that tissues and organs are adequately supplied

with oxygen and nutrients and that toxic metabolites are efficiently removed. Angiogenesis involves the release of growth factor gradients by inadequately supplied tissue, response to these factors mediated by receptors in surrounding vasculature, and proteases and adhesion molecules involved in tissue remodelling. Angiogenesis and neovascularization, inappropriate or abnormal angiogenesis, can be induced by a number of pathological conditions, usually in the context of hypoxia or inflammation.

As rapidly growing cell masses, solid tumors require a constant, plentiful supply of oxygen and nutrients. In larger tumors, perfusion is often inadequate, causing hypoxia and central necrosis. Various classes of compounds including inhibitors of signal transduction (i.e. LY333531), inhibitors of growth factor receptors (i.e. SU5416), protease inhibitors (i.e. KB-R7785, marimastat), and adhesion inhibitors (castanospermine) have shown activity in various models of angiogenesis and against multiple solid tumor types. Compounds showing promise in model systems or currently in development include the peptides aplidine, vascular endothelial growth inhibitor (VEGI), brain-specific angiogenesis inhibitor (BAI1), K1-5 (kringles 1-5 of plasminogen), U-995 (shark cartilage derived), endostatin, angiostatin, an antibody against vascular endothelial growth factor, and macrophage inflammatory protein 2 (MIP2, GRO2); the steroids and terpenoids squalamine, vitamin D3, and retinoic acid; the antibiotics clarithromycin and combretastatin A4; and the synthetic compounds SU5416 (Sugen), TNP-470, COL-3, IM862, PTK787/ZK222584 (Zeneca), CT-2584, KB-R7785, LY333531 (Eli Lilly), BPHA (Shionogi), carboxyamidotriazole, 5,6-dimethylxanthenone-4-acetic acid, and alpha-difluoromethylornithine, an inhibitor of polyamine synthesis.

II. *Current Indications for Angiogenesis Inhibitors*

Clinical trials of antiangiogenesis agents are underway for a wide variety of refractory and recurrent solid tumor types including Kaposi's sarcoma, non-Hodgkin's lymphoma, astrocytoma, glioblastoma, oligodendroglioma, ovarian, prostate, and renal tumors.

III. *Impact of Genotyping on Drug Development for Angiogenesis Inhibitors*

Vascular endothelial growth factor (VEGF) gene expression is increased in k-RAS transformed colorectal cells and VEGF expression is required for efficient tumor formation in nude mice but not for cell immortality. VEGF expression is associated with the progression, invasion and metastasis of colorectal cancer and overexpression of VEGF mRNA in the primary tumour is closely correlated with poor prognosis. High pretreatment serum VEGF is associated with poor response to

treatment and unfavorable survival in patients with small cell lung cancer treated with cisplatin and etoposide combination chemotherapy. These findings suggest the importance of this growth factor in tumor proliferation and implicate polymorphisms in VEGF proteins and VEGF receptor as potentially important determinants of prognosis, treatment efficacy, and toxicity.

The plasminogen-derived antiangiogenic peptide, angiostatin binds vitronectin and induces focal adhesion kinase (FAK1) activity in cell culture. FAK1 normally becomes phosphorylated only in response to cell-cell contact or treatment with peptide hormones including cholecystokinin, bombesin, and vasopressin. This observation suggests that the biological effects of angiostatin may relate to subversion of adhesion plaque formation in endothelial cells. The collagen XVIII-derived antiangiogenic peptide, endostatin binds fibulins 1 and 2 and also induces FAK1 activity.

Macrophage metalloproteinase (HME/MMP12) expression levels in hepatocellular tumors correlate well with angiostatin levels, which in turn were inversely correlated with poor survival. Transforming growth factor-beta 1, a key mediator of tumor angiogenesis, inhibits the generation of angiostatin in a pancreatic carcinoma cell line through modulation of the plasminogen activator/plasminogen activator inhibitor system. Generation of angiostatin may also involve an as yet unidentified, secreted disulfide reductase.

Polymorphisms in genes listed above or in Tables 1-3 and including similar genes not yet discovered that encode vascular growth factors, their receptors, and in enzymes involved in their processing that affect enzyme amounts, activity, or interaction with drug molecules could potentially affect neoplastic disease risk and prognosis as well as antiangiogenic treatment efficacy and toxicity.

Example 42

Protease Inhibitors

I. Description of Protease Inhibitors

Extracellular proteases play a crucial role in normal tissue remodeling during embryogenesis, growth, and wound healing by modulating the maturation and degradation of growth factors and extracellular matrix components such as elastin and collagen. Proteases play a role in angiogenesis—the potent inhibitors angiostatin and endostatin are proteolytic fragments of plasminogen and collagen 18A1, respectively. Extracellular proteases are involved in the progression of multiple pathological conditions such as osteoporosis and multiple inflammatory disorders including rheumatoid arthritis, multiple sclerosis, and nephritis.

Tumor metastasis, the migration of cells from the primary tumor to distal sites via the lymph or blood vessels, is mechanistically similar to the migration of lymphocytes from the lymph nodes to sites of inflammation, a process known to rely on the action of zinc requiring matrix metalloproteases (MMPs) and to be regulated by corresponding tissue inhibitors of metalloproteinases (TIMPs). Both matrix metalloproteases and their inhibitors occur in large, dispersed multigene families. Levels of MMP 1 and TIMP 1 correlate with metastatic potential and poor treatment outcome in breast, gastric, and colorectal cancers; levels of MMP 2 and TIMP 2 correlate with metastatic potential and poor treatment outcome in renal, urothelial, bladder, and colorectal cancers. Invasion of smooth muscle cell layers by tumor cells is inhibited by TIMPs and transfection of human breast cancer cells with TIMP4 reduces their growth and metastatic potential, suggesting direct involvement of metalloproteases in metastasis.

Several matrix metalloprotease have shown promising activity in tissue culture and *in vivo* models of metastasis including biphenyl sulfonyl-phenylalanine hydroxamic acid (BPHA), KB-R7785, and R-94138; several inhibitors including marimastat, batimastat, and AG3340 (Agouron) are in various stages of clinical development.

II. *Current Indications for Protease Inhibitors*

Clinical trials of protease inhibitors in progress target advanced lung cancers including small cell and non-small cell; supratentorial glioblastoma multiforme; gliosarcoma; gastric, pancreatic, and metastatic breast cancers; and combination therapy with mitoxantrone and prednisone for hormone refractory prostate cancer. Batimastat has shown promise for the treatment of malignant pleural effusion.

Because proteinase inhibitors are not cytotoxic, their use in anticancer therapies has been in combination with cytotoxic agents such as anthracycline antibiotics, microtubule inhibitors, topoisomerase inhibitors, etc., where they inhibit tumor growth indirectly through their antiangiogenic effects and tumor metastasis directly by inhibition of enzymes required for tumor dispersion.

As metalloproteases have been implicated in tumor metastasis, protease inhibitors may find widespread application for the prophylactic treatment of primary tumors during standard chemotherapeutic regimens to prevent the migration of (resistant) tumor cells to secondary sites.

III. *Limitations of Current Therapies Utilizing Protease Inhibitors*

Symptoms reported by patients with various malignancies during trials of marimastat included severe joint and muscle pain which were debilitating in >60%

of patients at doses >50 mg twice daily. These symptoms were reversible on discontinuation of the drug, and their incidence was been decreased by reducing the dose to 10 mg twice daily.

5 IV. *Impact of Genotyping on Drug Development for Protease Inhibitors*

Protease inhibitors have great potential in the treatment of neoplastic disease through their apparent ability to inhibit tumor invasion and dispersion. The protease/protease inhibitor systems that have been implicated in this process include the matrix metalloproteinases (MMPs) and their corresponding tissue inhibitors of metalloproteinase (TIMPs), the cathepsins (CTSs), and plasminogen activator (PLAU), plasminogen activator receptor (PLAUR), and plasminogen activator inhibitor (PAI1). As proteases are also involved in the inhibition of the angiogenesis required for tumor growth by releasing the potent inhibitors of angiogenesis, endostatin and angiostatin from collagen and plasminogen, greater understanding of the protease biology involved in these opposing processes will be required before protease inhibitor therapy can realize its full potential.

Serum levels of PLAU, PAI1, and PLAUR are predictors of progression and prognosis in prostate and gastric cancers: higher levels correlate with poor outcome and prophylactic chemotherapy after resection may be warranted for patients displaying high levels. Similarly, the five year relapse rate of patients having node-negative breast cancer with low PAI1 and low cathepsin D (CSTD) was 13% while patients who had greater than the median value for both of these molecules had a 5 year relapse rate of 40%. These data would indicate that at least two different protease systems are active in spread of node negative breast cancer and that measurement of CSTD and PAI1 levels may aid in the decisions to be made when offering adjuvant treatment to these patients. Cathepsin B (CTSB) is overexpressed in tumors of the lung, prostate, colon, breast, and stomach. Abundant extracellular expression of CTSB protein was found in 29 of 40 (72.5%) of esophageal adenocarcinoma specimens by use of immunohistochemical analysis.

A single nucleotide insertional polymorphism at -1607 in the promoter of matrix metalloproteinase 1 (MMP1), where an additional guanine (G) creates an Ets transcription factor binding site, creates an allele that displays significantly higher transcription in normal fibroblasts and in melanoma cells. This polymorphism occurs in the normal population with a frequency of 30%. In contrast, in eight tumor cell lines, this frequency increased to 62.5% ($P < 0.0001$), perhaps because increased levels of MMP1 allow more aggressive matrix degradation, thereby facilitating cancer progression.

Polymorphisms in genes listed above or in Tables 1-3 and including similar genes not yet discovered that encode proteases, their substrates (including adhesion proteins), their inhibitors, and in enzymes involved in their processing that affect enzyme amounts, activity, or interaction with drug molecules could potentially affect neoplastic disease risk and prognosis as well as protease inhibitor treatment efficacy and toxicity.

Example 43

Use of Genotype Information for the Identification of Candidates for Prophylactic Therapy

i) Occult Disease Detection and Prophylaxis

The early detection and treatment of neoplastic disease greatly improves prognosis—the prognosis for breast cancer chemotherapy is inversely related to lymph node involvement. Genotyping of polymorphisms known to be associated with increased risk for neoplastic disease would warrant careful monitoring or prophylactic treatment. Patients and practitioners must carefully weigh the benefits and associated undesired toxicities of prophylactic treatment against the risk of disease onset and response to conventional therapies.

Great advances in linking genetic polymorphisms to cancer risk have been made in recent years. Most link polymorphisms in genes involved in drug and xenobiotic metabolism (primarily phase I metabolism) to the appearance of various cancers. As environmental risk factors can be controlled, they can be viewed as modulators of genetic polymorphisms involved in innate risk. These include, but are not restricted to, the genes in the table below, which are known to be polymorphic and polymorphisms have been linked to innate or environmentally induced cancer risk in the scientific literature.

Associated Polymorphic Gene					
Cancer	Name	GID	OMIM_ID	VGX_Symbol	
Bladder	GSTM1	J03819	138352	GEN-9D	8824515
	NAT2	D90041	243401	GEN-466	10510890
	CYP2D6	X08007	124031	GEN-1FE	8824515
Breast	CYP17	M14564	202110	GEN-2Z	99415566 10519398 10404084 9950238 9067272

	CYP1A1	K03191	108330	GEN-9E	10468307 10519398
	COMT	M58525	116790	GEN-3S	10519398
	NAT2	D90040	243400	GEN-465	10389748
	HRAS	J00277	190020	GEN-MH8	8385520
	VDR	J03258	601769	GEN-2J	10344739 9613456
Colorectal	MTR	U73338	156570	GEN-69	10498402
	NAT1	D90042	108346	GEN-465	7627961
	APC	M74088	175100	GEN-3MW	9973276 9869603
	GSTM1	J03818	138351	GEN-9D	10445390
	HRAS	J00279	190022	GEN-MH10	2887194
	MTHFR	U09806	236250	GEN-4FZ	9067278 8895734

Associated Polymorphic Gene					
Cancer	Name	GID	OMIM_ID	VGX_Symbol	
Gastric	NAT1	D90043	108347	GEN-466	10585581
	MYCL1	M19720	164850	GEN-MK0	9635822
	MUC6	U97698	158374	GEN-LTG	9419405
	MUC1	X52228	158340	GEN-33N	9076520
Glioma	RB1	M33647	180200	GEN-2K1	9210953
Lung	CYP1A1	K03191	108330	GEN-9E	9610791 10506106
	DIA4	J03934	125860	GEN-12L	10397241 8528266
	MPO	X04876	254600	GEN-PS	9371491
	GSTM1	J03817	138350	GEN-9D	10506106 7728947
	MYCL1	M19721	164851	GEN-MK1	1345822
	GSTM3	J05459	138390	GEN-17O	7728947
	OGG1	Y13277	601982	GEN-9O	9935223
Melanoma	HRAS	J00278	190021	GEN-MH9	2572539
Myeloid Leukemia	IFNB	V00546	147640	GEN-TV	7912973
Oral	GSTP1	X06547	134660	GEN-19N	10376763
	CYP2D6	X08006	124030	GEN-1FE	9825835
Ovarian	EPHX	L25878	132810	GEN-29Z	8944076
Prostate	CYP17	M14564	202110	GEN-2Z	10469617
	NAT1	D90041	108345	GEN-464	10211944
	VDR	J03259	601770	GEN-2J	8797574
Testicular	WT1	X51630	194070	GEN-32A	8056449

Table: Polymorphic Genes Linked to Cancer Risk. Column 1, labelled "Cancer" shows commonly observed neoplastic diseases classified by organ or cell-type. Genes for which polymorphisms are linked to cancers listed in column 1 are under the broad heading "Associated Polymorphic Gene." These genes are identified by systematic name, "Name;" Genebank identifier, "GID;" Online Mendelian Inheritance in Man identifier, "OMIM_ID;" and internal, Variagenics, Inc. identifier, "VGX_Symbol." In addition, the PubMed database identifier, "PMID," allowing identification of pertinent literature is also given. Worldwide web addresses for the databases mentioned are in the "DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS" section under the subheading "Online Databases."

It is likely that the interplay of multiple polymorphic and non-polymorphic genes is involved in the process of neoplastic transformation with both positive and negative risk associations. But, a patient having several predisposing factors for a given cancer type listed in column 1 of the table above will be at greater risk than a patient having fewer. For example, patients with polymorphisms in glutathione-S-transferase (GST) M3 that reduce expressed levels are more likely to develop lung cancer if they also express low levels of GST M1. One skilled in the art will recognize that knowledge of risk ratios associated with various gene polymorphisms and neoplastic diseases will allow medical practitioners to determine whether prophylactic treatment, including change of habits or environment, preventative chemotherapy, careful monitoring for signs of disease, and prophylactic surgery, are warranted and advisable. Multiple risk-associated allelic loci can be genotyped to direct a course of prophylactic treatment in much the same manner as a high cholesterol count in a blood test carries an increased risk of heart disease and may warrant treatment with a statin-type drug (HMGCoA inhibitor).

It will also be recognized by one skilled in the art that factors including age, sex (in the case of non-gender specific cancers), ethnic background, and environment (including diet, smoking, alcohol consumption, and diet) impact risk determinations and great care must be exercised in extrapolating from one population to another.

II. *Post-Treatment Prophylaxis*

Notes: Aim is to forestall onset of new disease after successful initial therapy--correlation of tumor genotype with metastatic potential.

KIP1 polymorphisms, WAF1 polymorphisms, EGFR polymorphisms, ERBB2 polymorphisms

5

Other Embodiments

The invention described herein provides a method for identifying patients with a risk of developing neurological disease or dysfunction by determining the patients allele status for a gene listed in Tables 1-6, 11-17, and 18-23 and providing a forecast of the patients ability to respond to or tolerate a given drug treatment. In particular, the invention provides a method for determining, based on the presence or absence of a polymorphism, a patient's likely response to drug therapies of neurological disease or dysfunction. Given the predictive value of the described polymorphisms a candidate polymorphism is likely to have a similar predictive value for other drugs acting through other pharmacological mechanisms. Thus, the methods of the invention may be used to determine a patient's response to other drugs including, without limitation, antihypertensives, anti-obesity, anti-hyperlipidemic, or anti-proliferative, antioxidants, or enhancers of terminal differentiation.

In addition, while determining the presence or absence of the candidate allele is a clear predictor determining the efficacy of a drug on a given patient, other allelic variants of reduced catalytic activity are envisioned as predicting drug efficacy using the methods described herein. In particular, the methods of the invention may be used to treat patients with any of the possible variances, e.g., as described in Table 3 of Stanton et al., U.S. Application No. 09/300,747.

In addition, while the methods described herein are preferably used for the treatment of human patients, non-human animals (e.g., dogs, cats, sheep, cattle and other bovines, swine, and apes and other non-human primates) may also be treated using the methods of the invention.

It will be readily apparent to one skilled in the art that varying substitutions and modifications may be made to the invention disclosed herein without departing from the scope and spirit of the invention. For example, using other compounds, and/or methods of administration are all within the scope of the present invention. Thus, such additional embodiments are within the scope of the present invention and the following claims.

The invention illustratively described herein suitably may be practiced in the absence of any element or elements, limitation or limitations which is not specifically disclosed herein. Thus, for example, in each instance herein any of the terms "comprising", "consisting essentially of" and "consisting of" may be replaced with either of the other two terms. The terms and expressions which have been employed are used as terms of description and not of limitation, and there is no intention that in the use of such terms and expressions of excluding any equivalents

of the features shown and described or portions thereof, but it is recognized that various modifications are possible within the scope of the invention claimed. Thus, it should be understood that although the present invention has been specifically disclosed by preferred embodiments and optional features, modification and
5 variation of the concepts herein disclosed may be resorted to by those skilled in the art, and that such modifications and variations are considered to be within the scope of this invention as defined by the appended claims.

In addition, where features or aspects of the invention are described in terms of Markush groups or other grouping of alternatives, those skilled in the art will
10 recognize that the invention is also thereby described in terms of any individual member or subgroup of members of the Markush group or other group.

Table 1. C. *logy* Gene List

Class	Pathway	Function	Name	OMIM	GID	Locus
Drug Uptake and Export (additional genes in Toxicology)	Transporter	Transporter	multidrug resistance associated protein MRP1	158343	L05628	16p13.1
			multidrug resistance associated protein MRP2/CMOAT	601107	NM_000392	10q24
			ATP-binding cassette, sub-family C (CFTR/MRP), member 3/CMOAT2	*****	NM_003786	*****
			ATP-binding cassette, sub-family C (CFTR/MRP), member 4/MOATB	*****	NM_005845	*****
			ATP-binding cassette, sub-family C (CFTR/MRP), member 5/SMRP	*****	NM_005688	*****
			ATP-binding cassette, sub-family C (CFTR/MRP), member 9/SUR2	601439	NM_005691	*****
			multidrug resistance protein MDR1	171050	X96395	7q21.1
			multidrug resistance protein MDR3/P-glycoprotein 3/P-gly	602347	X06181	7q21.1
			Human sorcin/SRI	182520	L12387	7q21.1
			Placenta-specific ATP-binding cassette transporter/ABCP	603756	NM_004827	4q22
			anthracene resistance-related protein/ARA	603234	NM_001171	16p13.1
			sulfonylurea receptor (hyperinsulinemia)/SUR	600509	NM_000352	11p15.1
			Solute carrier family 29, member 1/SLC29A1/ENT1	602193	NM_004955	6p21.2-p21.1
			Solute carrier family 29, member 2/SLC29A2/ENT2	602110	X86681	11q13
			Glutathione-S-transferase 6	138391	*****	*****

Drug Metabolism (additional genes in Toxicology)	Drug Inactivation (additional genes in Toxicology)	Glutathione				
		Glutathione-S-transferase, alpha 1/GSTA1	138359	L13269	6p12.2	
		Glutathione-S-transferase, alpha 2/GSTA2	138360	M15872	6p12.2	
		Glutathione-S-transferase, kappa 1/GSTK1	602321	*****	*****	
		Glutathione-S-transferase 1/MGST1 (microsomal)	138330	AH003674	Chr.12	
		Glutathione-S-transferase 2/MGST2 (microsomal)	601733	NM_00241 3	4q28-q31	
		Glutathione-S-transferase, mu 1- like/GSTM1L	138270	*****	Chr. 3	
		1/GSTM1	138350	J03817	1p13.3	
		Glutathione-S-transferase, mu 2/GSTM2 (muscle)	138380	NM_00084 8	1p13.3	
		Glutathione-S-transferase, mu 3/GSTM3 (brain)	138390	NM_00084 9	1p13.3	
		Glutathione-S-transferase, mu 4/GSTM4	138333	NM_00085 0	1p13.3	
		Glutathione-S-transferase, mu 5/GSTM5 (brain/lung)	138385	NM_00085 1	1p13.3	
		Glutathione-S-transferase, pi/GSTP1	134660	NM_00085 2	11q13	
		Glutathione-S-transferase, theta 1/GSTT1	600436	NM_00085 3	22q11.2	
		Glutathione-S-transferase, theta 2/GSTT2	600437	NM_00085 4	22q11.3	
		Glutathione-S-transferase, zeta 1/maleylacetoacetate isomerase/MAAI/GSTZ1	603758	NM_00151 3	14q24.3	

	glutathione reductase	138300	X15722	8p21.1
	glutathione peroxidase GPx2	138319	X68314	14q24.1:
	glutathione peroxidase GPx3	138321	X58295	5q32-q33.1
	glutathione peroxidase GPx1	138320	Y00433	3p21.3
	glutathione peroxidase GPx4	138322	X71973	19p13.3
	glutathione peroxidase GPx5	603435	AJ005277	*****
Metallo-thionein	metallothionein 2a	NM_00595	3	16q13
	metallothionein 1g	156360	J03910	16q13
	metallothionein 1f	156353	M10943	16q13
	metallothionein 1e	156352	M10942	16q13
	metallothionein 1b	156351	AH001510	16q13
	metallothionein 3	156349	NM_00595	16q13
Proteolysis	bleomycin hydrolase	139255	4	16q13
Methylation	thiopurine methyltransferase	602403	X92106	17q11.2
		187680	U12387	6p22.3
Oxidation	dehydrogenase/ALDH1	100640	M26761	9q21
	myeloperoxidase	254600	X04876	17q23.1
Acetylation	N-acetyltransferase 1/NAT1	NM_00066	2	8p23.1- p21.3
	N-acetyltransferase 2/NAT2	108345	NM_00001	8p23.1- p21.3
	human DNA mismatch repair protein hMLH1/MutL	243400	5	
	xeroderma pigmentosum complementation group A/XPA	120436	U07418	3p21.3
	xeroderma pigmentosum complementation group C/XPC	278700	D14533	9q22.3
		278720	NM_00462	3p25

RAD2 (<i>S. cerevisiae</i>) homolog/RAD2/excision repair complementation group 5/ERCC5	133530	NM_00012 3	13q33
RAD23 (<i>S. cerevisiae</i>) homolog A/RAD23A	600061	NM_00505 3	19p13.2
RAD23 (<i>S. cerevisiae</i>) homolog B/RAD23B	600062	NM_00287 4	3p25.1
RAD26 (<i>S. cerevisiae</i>) homolog/RAD26/excision repair complementation group 6/ERCC6	133540	NM_00012 4	10q11
RAD50 (<i>S. cerevisiae</i>) homolog/RAD50	604040	NM_00573 2	5q31
RAD51 (<i>S. cerevisiae</i>) homolog (E coli RecA homolog)/RAD51	179617	NM_00287 5	15q15.1
RAD51 (<i>S. cerevisiae</i>) homolog B/RAD51L1	602948	Y15572	14q23.3- q24
RAD51 (<i>S. cerevisiae</i>) homolog D/RAD51L2	602774	NM_00287 6	17q
RAD52 (<i>S. cerevisiae</i>) homolog/RAD52	602954	NM_00287 8	17q11
RAD51 (<i>S. cerevisiae</i>) homolog C/RAD51L4	600392	NM_00287 9	12p13- q12.2
RAD54 (<i>S. cerevisiae</i>)-like/RAD54L excision repair complementation group 1/ERCC1	603615	NM_00357 9	1p32
excision repair complementation group 2/ERCC2/XPD	126380	NM_00198 3	19q13.2- q13.3
excision repair complementation group 1/ERCC3/XPB	126340	L47234	19q13.2- q13.3
	133510	NM_00012 2	2q21

DNA Repair

DNA Replication and Repair	excision repair complementation group 4/ERCC4	133520	NM_00523 6	16p13.3- p13.13
	replication protein A1 (70kD)/RPA1	179835	NM_00294 5	17p13.3
	replication protein A2 (32kD)/RPA2	179836	NM_00294 6	1p35
	replication protein A3 (14kD)/RPA3	179837	NM_00294 7	7p22
	excision repair protein ERCC1	126380	M13194	19q13.2- q13.3
	mismatch repair protein hMSH2	120435	U03911	2p22-p21
	O6 alkylguanine-DNA alkyltransferase	156569	M60761	10q24.33- qter
	ADP-ribosyltransferase (NAD ⁺ ; poly (ADP-ribose) polymerase)/PARP/ADPRT	173870	NM_00161 8	1q42
	poly (ADP-ribose) glycohydrolase/PARG	603501	NM_00363 1	10q11.23
	APEX nuclease (multifunctional DNA repair enzyme)/APEX	107748	NM_00164 1	14q12
	8-oxoguanine DNA glycosylase/OGG1	601982	NM_00254 2	3p26.2
	N-methylpurine-DNA glycosylase/MPG	156565	NM_00243 4	16pter- p13.3
	topoisomerase IIb	126431	U54831	3p
	topoisomerase IIa	126430	J04088	17q21-q22;
	topoisomerase I	126420	J03250	20q12- q13.1

Replication

Mitosis	beta tubulin 2/TUBB2	602660	NM_006088	*****
	beta tubulin 4/TUBB4	602661	NM_006086	*****
	beta tubulin 5/TUBB5	602662	NM_006087	*****
	gamma tubulin/TUBG	191135	NM_001070	*****
Histone Acetylation	histone acetyltransferase			
	histone deacetylase	603053	AF030424	2q31.2-q33.1
		601241	U50079	1p34.1
Telomere Maintenance	telomerase protein component 1	601686	U86136	14q11.2
	telomerase reverse transcriptase	187270	AF015950	5p15.33
	telomerase RNA component	602322	U86046	3q21-q28
DNA Methylation	DNA methyltransferase DNMT1	126375	X63692	19p13.3-p13.2
	DNA methyltransferase DNMT2	602478	AF012128	10p15.1
	DNA methyltransferase DNMT3A	602769	AF067972	2p23
	DNA methyltransferase DNMT3B	602900	NM_006892	20q11.2
	thymidylate synthetase	188350	X02308	18p11.32
	cytidine deaminase	123920	L27943	1p36.2-p35
	DPD	274270	U09178	1p22
	deoxycytidine kinase	125450	M60527	4q13.3-q21.1
	Soluble thymidine kinase 1/TK1	188300	NM_003258	17q25.2-q25.3
	2/TK2	188250	U77088	Chr.16

Nucleotide Metabolism	Pyrimidines	uridine kinase	191730	NM_003364	Chr.7
		uridine monophosphate kinase	191710	NM_005267	1p32
Purines		uridine phosphorylase	191730	NM_003364	Chr.7
		thymidine phosphorylase	131222	M58602	22q13.32-qter
		aspartate transcarbamylase/CAD trifunctional protein	114010	NM_004341	2p21
		orotate phosphoribosyl transferase	258900	NM_000373	3q13
		hypoxanthine-guanine phosphoribosyltransferase	308000	M31642	Xq26-q27.2
		adenosine phosphoribosyltransferase/APRT	102600	NM_000485	16q24
		thiopurine S-methyltransferase/TPMT	187680	NM_000367	6p22.3
		urate oxidase	191540	AH003594	1p22
		adenylosuccinate synthetase/ADSS	103060	NM_001126	1cen-q12
		adenylosuccinate lyase	103050	NM_000026	22q13.1
		glycinamide ribotide formyltransferase	138440	X54199	21q22.1
		purine nucleoside phosphorylase	164050	NM_000270	14q13.1
		xanthine oxidase	278300	NM_000379	2p23-p22
		adenosine deaminase	102700	NM_000022	20q13.11

Cellular Metabolism	Ribo-nucleotides	ribonucleotide reductase M1 subunit	180410	L10342	11p15.5
		ribonucleotide reductase M2 subunit	180390	X59618	2p25-p24
		ecto-5'-nucleotidase (CD73)/NT5	129190	X55740	6q14-q21
	General	alkaline phosphatase	171760	NM_000478	1p36.1-p34
		asparagine synthetase	108370	M27396	7q21-q31
		arginase (ARG1)	207800	M14502	*****
	Amino Acid Metabolism	arginase (ARG2)	107830	D86724	14q24.1-q24.3
		ornithine transaminase	258870	NM_000274	10q26
		cytochrome P450 aromatase (CYP19)	107910	X13589	15q21.1
	Steroid Metabolism (additional genes in Endocrinology and Metabolism)	steroid 5 alpha reductase	184753	M32313	5p15
		estrogen sulfotransferase	600043	U20521	4q13.1
		steroid 5-alpha reductase 2	264600	NM_000348	2p23
		HMGCoA reductase	142910	NM_000859	5q13.3-q14
		squalene synthetase	184420	X69141	8p23.1-p22
		Folate Receptor Alpha/FOLR1	136430	M28099	1q13.3-q13.5
Folate Receptor Beta/FOLR2		136425	AF000380	1q13.3-q13.5	
Folate Receptor Gamma/FOLR3		602469	Z32564	*****	
Folate Transporter (SLC19A1)		600424	U19720	21q22.3	
Vitamin B12 binding protein		275350	NM_000355	22q11.2-qter	
folylpolyglutamate synthetase/FPGS		136510	M98045	9cen-q34	
gamma-glutamyl hydrolase/GGH		601509	U55206	*****	
Methylenetetrahydrofolate reductase/MTHFR	236250	U09806	1p36.3		
Dihydrofolate reductase/DHFR	126060	J00140	5q11.2-q13.2		

Folate Metabolism	Folate Metabolism	5,10-methylenetetrahydrofolate dehydrogenase, 5,10- methylenetetrahydrofolate cyclohydrolase, 10- formyltetrahydrofolate synthetase/MTHFD1	172460	NM_005956	14q24
		5,10-methylenetetrahydrofolate synthetase (5-formyltetrahydrofolate cyclo-ligase)/MTHFS	604197	NM_006441	Chr. 15
		phosphoribosylglycinamide formyltransferase, phosphoribosylglycinamide synthetase,			
		phosphoribosylaminoimidazole folate hydrolase 1/FOH1	138440	NM_000819	21q22.1
		6-pyruvoyl tetrahydrobiopterin synthase/PTPS	600934	NP_004467	11q14
		serine hydroxymethyltransferase 1 (soluble)/SHMT1	261640	Q03393	1q22.3-q23.3
		serine hydroxymethyltransferase 2 (mitochondrial)/SHMT2	182144	NM_004169	17p11.2
		Glycine aminotransferase/glycine cleavage T protein/GAT	138450	NM_005412	12q13
		5-methylenetetrahydrofolate- homocysteine methyltransferase/methionine glutamate	238310	NM_000481	3p21.2-p21.1
		formiminotransferase/dihydrofolate synthetase	156570	NM_000254	1q43
			229100	*****	*****

Protein Modification	Prenylation	farnesyl:protein transferase alpha/FNTA	134635	NM_002027	8p22-q11
		farnesyl:protein transferase beta/FNTB	134636	NM_005023	14q23-q24
		Rab geranylgeranyltransferase, alpha subunit/RABGGTA	601905	NM_004581	14q11.2
		Rab geranylgeranyltransferase, beta subunit/RABGGTB	179080	NM_004582	1p31-p22
Polyamine Metabolism	Polyamine Metabolism	ornithine decarboxylase 1 (ODC1)	165640	M16650	2p25
		SAM decarboxylase	180980	M21154	6q21-q22
Phospholipid Metabolism	Phospholipid Metabolism	glucosylceramide synthase	602874	D50840	9q31
		interferon alpha1 (IFNa1)	147660	X02956	9p22
		interferon alpha2 (IFNa2)	147562	*****	9p22
		interferon beta1 (IFNb1)	147640	V00546	9p21
		interferon beta3 (IFNb3)	147860	*****	Chr.8
		interferon omega1 (IFNw1)	147553	X02669	9p21
		interferon gamma (IFNg)	147570	L07633	12q14
		interleukin 1 alpha (IL1a)	147760	M15329	2q14
		interleukin 1 beta (IL1b)	147720	K02770	2q14
		interleukin 2 (IL2)	147680	X01586	4q26-q27
		interleukin 3 (IL3)	147740	M20137	5q31.1
		interleukin 4 (IL4)	147780	M13982	5q31.1
		interleukin 5 (IL5)	147850	X04688	5q31.1
		interleukin 6 (IL6)	147620	M14584	7p21
		interleukin 7 (IL7)	146660	J04156	8q12-q13
		interleukin 8 (IL8)	146930	M26383	4q12-q13
		interleukin 9 (IL9)	146931	X17543	5q31.1
		interleukin 10 (IL10)	124092	M57627	1q31-q32

interleukin 11 (IL11)	147681	X58377	19q13.3-q13.4
interleukin 12a (IL12a)	161560	NM_002187	3p12-q13.2
interleukin 12b (IL12b)	161561	NM_000440	5q31.1-q33.1
interleukin 13 (IL13)	147683	X69079	5q31
interleukin 15 (IL15)	600554	U14407	4q31
interleukin 16 (IL16)	603035	NM_004513	*****
interleukin 18 (IL18)	600953	*****	11q22.2-q22.3
interferon alpha receptor 1 (IFNAR1)	107450	X77722	21q22.1
interferon alpha receptor 2 (IFNAR2)	147569	U68755	21q22.1-q22.2
(IFNGR1)	107470	J03143	6q23-q24
interferon gamma receptor 2 (IFNGR2)	602376	NM_000874	21q22.1
interleukin 1 receptor 1 (IL-1R1)	147810	M27492	2q12
interleukin 1 receptor 2 (IL-1R2)	147811	NM_004633	2q12-q22
interleukin 2 receptor alpha (IL-2Ra)	147730	X01057	10p15-p14
interleukin 2 receptor beta (IL-2Rb)	146710	M26062	22q11.2-q13
interleukin 2 receptor gamma (IL-2Rg)	308380	D11086	Xq13
interleukin 3 alpha receptor (IL-3aR)	308385	M74782	Xp22.3
interleukin 4 receptor (IL-4R)	147781	X52425	16p12.1-p11.2
interleukin 5 receptor alpha (IL-5Ra)	147851	M96652	3p26-p24;
interleukin 6 receptor (IL-6R) (20)	147880	X12830	1q21

Cytokines

interleukin 7 receptor (IL-7R)	146661	M29696	5p13
interleukin 8 receptor alpha (IL-8Ra)	146929	M68932	2q35
interleukin 8 receptor beta (IL-8Rb)	146928	M94582	2q35
interleukin 9 receptor (IL-9R)	300007	M84747	Xq28
10Ra)	146933	U00672	11q23.3
interleukin receptor 11 alpha (IL-11a)	600939	U32324	9p13
interleukin receptor 12 beta (IL-12b)	600939	U03187	9p13
12b2)	601642	U03187	1p31.2
interleukin receptor 13 alpha (IL-13a)	300119	S80963	Chr.X
13a2)	300130	X95302	Xq24
15Ra)	601070	U31628	10p15-p14
tumor necrosis factor alpha/TNFA	191160	X01394	6p21.3
tumor necrosis factor beta/TNFB/lymphotoxin alpha/LTA	153440	NM_00059 5	6p21.3
tumor necrosis factor ligand superfamily, member 4/TNFSF4	603594	NM_00332 6	1q25
tumor necrosis factor ligand superfamily, member 5/TNFSF5	308230	NM_00007 4	Xq26
tumor necrosis factor ligand superfamily, member 6/TNFSF6	134638	*****	1q23
tumor necrosis factor ligand superfamily, member 7/TNFSF7	602840	NM_00125 2	19p13
tumor necrosis factor ligand superfamily, member 8/TNFSF8	603875	NM_00124 4	9q33
tumor necrosis factor ligand superfamily, member 10/TNFSF10	603598	NM_00381 0	3q26
tumor necrosis factor ligand superfamily, member 11/TNFSF11	602642	NM_00370 1	13q14
tumor necrosis factor ligand superfamily, member 12/TNFSF12	602695	NM_00380 9	17p13.3

Inflammation
(additional
genes in
Immunology)

Inflammation (additional genes in Immunology)	tumor necrosis factor ligand superfamily, member 13B/TNFSF13B	603969	NM_006573	13q32-q34
	tumor necrosis factor ligand superfamily, member 15/TNFSF15	604052	*****	9q33
	macrophage inflammatory protein 1 alpha	182283	M23178	17q11-q21
	tumor necrosis factor ligand superfamily, member 18/TNFSF18	603898	*****	1q23
	myeloid progenitor inhibitory factor 1	602494	*****	*****
	macrophage inflammatory protein 1 alpha	182283	M23178	17q11-q21
	2',5'-oligoadenylate synthetase 1 (OAS1)	164350	NM_006187	12q24.2
	2',5'-oligoadenylate synthetase 2 (OAS2)	603350	M87284	12q24.2
	2',5'-oligoadenylate synthetase 3 (OAS3)	603351	*****	12q24.2
	arachidonate 5' lipoxygenase/ALOX5	152390	J03571	Chr.10
Interferon Response	arachidonate 12-lipoxygenase/ALOX12	152391	NM_000697	17p13.1
	prostaglandin endoperoxide synthetase 1/COX1/PTGS1	176805	AH001520	9q32-q33.3
	prostaglandin endoperoxide synthetase 2/COX2/PTGS2	600262	NM_000963	1q25.2-q25.3
	thromboxane A synthase 1/TBXAS1	274180	SEG_D34613S	7q34
	prostaglandin D2 synthase	602598	M61900	*****
	prostaglandin I2 synthase/prostacyclin synthase/PTGIS	601699	SEG_D83393S	20q13

Prostaglandin	prostaglandin E receptor 1, EP1 subtype/PTGER1	176802	NM_000955	19p13.1
	prostaglandin E receptor 2, EP2 subtype/PTGER2	176804	*****	5p13.1
n	prostaglandin E receptor 3, EP3 subtype/PTGER3	176806	NM_000957	1p31.2
	prostaglandin E receptor 4, EP4 subtype/PTGER4	601586	NM_000958	5p13.1
	prostaglandin F receptor/PTGFR	600563	L24470	1p31.1
	prostaglandin F2 receptor negative regulator/PTGFRN	601204	U26664	1p13.1-q21.3
	prostaglandin I2 receptor/PTGIR/prostacyclin receptor	600022	SEG_HUM IP	19q13.3
	15-hydroxyprostaglandin dehydrogenase/HPGD	601688	NM_000860	4q34-q35
	aldo-keto reductase family 1, member C2/AKR1C2	600450	NM_001353	10p15-p14
	integrin alpha 1	192968	Y00796	Chr.5
	integrin alpha 2	192974	X17033	5q23-q31
	integrin alpha 4	192975	L12002	2q31-q32
	integrin alpha 5	135620	NM_002205	12q11-q13
	integrin alpha 6	147556	X59512	Chr.2
	integrin alpha 7	600536	AF032108	12q13
	integrin alpha 8	604063	L36531	*****
	integrin alpha 9	603963	L24158	*****
	integrin alpha 10	604042	AF074015	*****
	integrin alpha D	602453	U40279	16p11.2
	integrin alpha M	120980	J04145	16p11.2

Adhesion	Integrins	integrin alpha X	151510	M81695	16p11.2
		integrin beta 1	135630	U28252	10p11.2
		integrin beta 2	600065	M15395	21q22.3
		integrin beta 3	173470	M35999	17q21.32
		integrin beta 4	147557	X51841	17q11-qter
		integrin beta 5	147561	M35011	*****
		integrin beta 6	147558	M35198	Chr.2
		integrin beta 7	147559	M68892	12q13.13
		integrin beta 8		NM_00221	
			604160	4	*****
		cadherin 2/NCAD/CDH2	114020	Z27440	18q11.2
		human cell adhesion protein SQM1	603842	NM_00414	19p13.12-
				6	p13.11
	Proteases	matrix metalloproteinase 3, stromelysin 1	185250	NM_00242	2
		matrix metalloproteinase 1, aminopeptidase A/glutamyl aminopeptidase/ENPEP	120353	M13509	11q22-q23
		mammary serine protease/protease M/neurosin	138297	L14721	4q25
			602652	D78203	19q13.3
		protease inhibitor 5/maspin	154790	NM_00263	9
		activator	191840	AH007073	18q21.3
		cathepsin B	116810	M14221	10q24
				8p22	
		type 2 plasminogen activator inhibitor	173390	NM_00257	5
		urokinase-type plasminogen activator receptor	173391	NM_00265	9
					18q21.3
					19q13

RAD1 (S. pombe) homolog/RAD1	603153	NM_002853	5p13.3-p13.2
RAD9 (S. pombe) homolog/RAD9	603761	NM_004584	11q13.1-q13.2
RAD17 (S. pombe) homolog/RAD17	603139	NM_002873	4q13.3-q21.2
FRAP-related protein/FRP1/ATR	601215	U49844	3q22-q24
HUS1 (S. pombe) checkpoint homolog/HUS1	603760	NM_004507	7p13-p12
ataxia telangiectasia mutated (complementation groups A, C and D)/ATM	208900	NM_000051	11q22.3
CHK1 (checkpoint, S.pombe) homolog/CHEK1	603078	NM_001274	11q22-q23
growth arrest and DNA-damage-inducible, alpha/GADD45A	126335	NM_001924	1p34-p12
BRCA1	113705	NM_000058	17q21
BRCA2	600185	NM_000059	13q12.3
benzimidazoles 1 (yeast homolog)/BUB1	602452	AF139363	2q12-q14
benzimidazoles 1 (yeast homolog), beta/BUB1B	602860	NM_001211	15q14-q21
benzimidazoles 1 (yeast homolog)/BUB3	603719	NM_004725	10q24-q26
MAD (mothers against decapentaplegic) homolog 1/MADH1	601595	NM_005900	4q28
MAD (mothers against decapentaplegic) homolog 2/MADH2	601366	NM_005901	18q21

**DNA
Damage
Checkpoint**

MAD (mothers against decapentaplegic) homolog 3/MADH3	603109	NM_00590 2	15q21-q22
MAD (mothers against decapentaplegic) homolog 4/MADH4	600993	NM_00535 9	18q21.1
MAD (mothers against decapentaplegic) homolog 5/MADH5	603110	NM_00590 3	5q31
MAD (mothers against decapentaplegic) homolog 6/MADH6	602931	NM_00558 5	15q21-q22
MAD (mothers against decapentaplegic) homolog 7/MADH7	602932	NM_00590 4	Chr.18
MAD (mothers against decapentaplegic) homolog 9/MADH9	603295	NM_00590 5	13q12-q14
cyclin-dependent kinase (CDK2)	116953	NM_00179 8	12q13
cyclin-dependent kinase (CDK3)	123828	NM_00125 8	17q22-qter
cyclin-dependent kinase (CDK4)	123829	NM_00007 5	12q14
cyclin-dependent kinase (CDK5)	123831	NM_00493 5	7q36
cyclin-dependent kinase (CDK6)	603368	NM_00125 9	7q21-q22
cyclin-dependent kinase (CDK7)	601955	NM_00315 7	2p15-cen
cyclin-dependent kinase (CDK8)	603184	NM_00126 0	13q12
cyclin-dependent kinase (CDK9)	603251	NM_00126 1	9q34.1
cyclin A1	604036	U66838	*****
cyclin A2	123835	X51688	4q27

cyclin B1	123836	M25753	5q12
cyclin B2	602755	AF002822	*****
cyclin C	123838	M74091	6q21
cyclin D1	168461	M73554	11q13
cyclin D2	123833	M90813	12p13
cyclin D3	123834	M90814	6p21
cyclin E1	123837	U40739	19q13.1
cyclin E2	603775	AF091433	*****
cyclin F	600227	Z36714	16p13.3
cyclin G1	601578	X77794	5q32-q34
cyclin G2	603203	U47414	*****
cyclin H	601953	U11791	5q13.3-q14
cyclin K	603544	AF060515	14q32
cyclin T1	602506	AF045161	Chr.12
cyclin T2	603862	AF048731	*****
cyclin-dependent kinase inhibitor 1a/WAF	116899	U03106	6p21.2
cyclin-dependent kinase inhibitor 1b/KIP1	600778	U10906	12p13
cyclin-dependent kinase inhibitor 2a	600160	NM_00007 7	9p21
cell cycle CDC2	116940	NM_00178 6	10q21.1
cell division cycle 25A/CDC25A	116947	NM_00178 9	3p21
E2F transcription factor 1/E2F1	189971	M96577	20q11.2
E2F transcription factor 2/E2F2	600426	NM_00409 1	1p36
E2F transcription factor 3/E2F3	600427	NM_00194 9	6p22

Cell Cycle

E2F transcription factor 4/E2F4	600659	NM_001950	16q22.1
E2F transcription factor 5/E2F5	600967	NM_001951	*****
E2F transcription factor 6/E2F6	602944	NM_001952	*****
transcription factor Dp-1 (E2F dimerization partner 1)/TFDP1	189902	NM_007111	13q34
transcription factor Dp-2 (E2F dimerization partner 2)/TFDP2	602160	NM_006286	3q23
retinoblastoma-related gene RB2/p130	180203	NM_005611	16q12.2
retinoblastoma RB1	180200	NM_000321	13q14.1-14.2
insulin-like growth factor 1/somatomedin C/IGF1	147440	M11568	12q22-q24.1
insulin-like growth factor 2/somatomedin A/IGF2	147470	NM_000612	11p15.5
insulin-like growth factor binding protein 1	146730	NM_000596	7p14-p12
insulin-like growth factor binding protein 2	146731	X16302	2q33-q34
insulin-like growth factor binding protein 3	146732	NM_000598	7p14-p12
insulin-like growth factor binding protein 4	146733	M62403	17q12-q21
insulin-like growth factor binding protein 5	146734	L27560	*****
insulin-like growth factor binding protein 6	146735	M69054	Chr.12

insulin-like growth factor binding protein 7	602867	L19182	4q12
insulin-like growth factor binding protein 10	602369	U62015	1p22.3
schwannoma-derived growth factor/amphiregulin/AREG	104640	NM_001657	4q13-q21
trefoil factor 1/sP2	113710	X00474	21q22.3
trefoil factor 2/TFF2	182590	X51698	21q22.3
trefoil factor 3/sP2	600633	L08044	21q22.3
epidermal growth factor EGF	131530	X04571	4q25
transforming growth factor (TGF-B1)	190180	M60315	19q13.1-q13.3
transforming growth factor (TGF-B2)	190220	M19154	1q41
transforming growth factor (TGF-B3)	190230	X14149	14q24
vascular endothelial growth factor (VEGF-A)	192240	M32977	6p12
vascular endothelial growth factor (VEGF-B)	601398	U52819	11q13
vascular endothelial growth factor (VEGF-C)	601528	X94216	*****
erythropoietin/EPO	133170	NM_000799	7q21
cardiotrophin 1	600435	*****	*****
leukemia inhibitory factor/LIF	159540	NM_002309	22q12.1-q12.2
ciliary neurotrophic factor/CNTF	118945	NM_000614	11q12.2
oncostatin M	165095	*****	22q12.1-q12.2
heparin-binding growth factor 1/FGF1	131220	AH002717	5q31

Growth Factors

basic fibroblast growth factor/FGF2	134920	M27968	4q25-q27
fibroblast growth factor 3/FGF3	164950	NM_005247	11q13
HST oncogene/fibroblast growth factor 4/FGF4	164980	NM_002008	11q13
fibroblast growth factor-related protein/FGF5	165190	AH005423	4q21
fibroblast growth factor 6/FGF6	134921	X63454	12p13
keratinocyte growth factor/fibroblast growth factor 7/FGF7	148180	L06245	15q15-q21.1
fibroblast growth factor 8 (androgen-induced)/FGF8	600483	NM_006119	10q24
fibroblast growth factor 9 (glia-activating factor)/FGF9	600921	NM_002010	13q11-q12
fibroblast growth factor 10/FGF10	602115	NM_004465	5p13-p12
fibroblast growth factor 11/FGF11	601514	NM_004112	17q21
fibroblast growth factor 12/FGF12	601513	*****	3q28
fibroblast growth factor 13/FGF13	300070	*****	Xq26.3
fibroblast growth factor 14/FGF14	601515	NM_004115	13q34
fibroblast growth factor 16/FGF16	603724	NM_003868	*****
fibroblast growth factor 17/FGF17	603725	NM_003867	8p21
fibroblast growth factor 18/FGF18	603726	NM_003862	*****
fibroblast growth factor 19/FGF19	603891	NM_005117	*****

stem cell factor/mast cell growth factor (MGF)	184745	NM_003994	12q22
thrombopoietin/THPO	600044	NM_000460	3q26.3-q27
platelet derived growth factor beta polypeptide/PDGFB/SIS	190040	NM_002608	22q12.3-q13.1
insulin-like growth factor 1 receptor precursor/IGF1R	147370	NM_000875	15q25-q26
insulin-like growth factor 2 receptor/IGF2R	147280	NM_000876	6q26
epidermal growth factor receptor EGFR	131550	NM_005228	7p12.3-p12.1
tyrosine kinase-type cell surface receptor HER2/ERBB2/NEU	164870	X03363	17q21.2
glucocorticoid receptor	138040	M11050	5q31
glucocorticoid receptor alpha	138040	U25029	5q31
glucocorticoid receptor beta	138040	X03348	5q31
progesterone receptor	264080	M15716	11q22
androgen receptor	313700	M20132	Xq11-q12
estrogen receptor 1 (ESR1)	133430	M12674	6q25.1
estrogen receptor 2 (ESR2)	601663	X99101	14q
retinoic acid receptor alpha (RARA)	180240	X06538	17q12
retinoic acid receptor beta (RARB)	180220	X07282	3p24
retinoic acid receptor gamma (RARG)	180190	M38258	12q13
Peroxisome proliferative activated receptor, alpha/PPARA	170998	NM_005036	22q12-q13.1
Peroxisome proliferative activated receptor, gamma/PPARG	601487	NM_005037	3p25
Peroxisome proliferative activated receptor, delta/PPARD	180231	NM_006223	1q21.3

c-kit (MGF receptor)	164920	X06182	4q12
TGF-B type I receptor	190181	AH006005	9q33-q34
TGF-B type II receptor	190182	NM_00324 2	3p22
TGF-B type III receptor	600742	L07594	1p33-p32
fibroblast growth factor receptor 1/FGFR1	136350	*****	8p11.2- p11.1
fibroblast growth factor receptor 2/FGFR2	176943	Y17131	10q26
fibroblast growth factor receptor 3/FGFR3	134934	NM_00524 7	4p16.3
fibroblast growth factor receptor 4/FGFR4	134935	NM_00201 1	5q35.1-qter
VEGF receptor	191306	X61656	4q12
mitogen activated protein kinase PRKM1/MAPK1	176948	NM_00274 5	22q11.2
mitogen activated protein kinase PRKM3/MAPK3	601795	X60188	16p11.2
mitogen activated protein kinase PRKM4/MAPK4	176949	NM_00274 7	18q12-q21
mitogen activated protein kinase PRKM6/MAPK6	602904	NM_00274 8	*****
mitogen activated protein kinase PRKM7/MAPK7	602521	NM_00274 9	17p11.2
mitogen activated protein kinase JNK1/PRKM8/MAPK8	601158	L26318	*****
mitogen activated protein kinase JNK2/PRKM9/MAPK9	602896	U09759	5q35
mitogen activated protein kinase JNK3/PRKM10/MAPK10	602897	U35003	*****

mitogen activated protein kinase PRKM11/MAPK11	602898	AF031135	*****
mitogen activated protein kinase SAPK3/MAPK12	602399	NM_00296 9	22q13.3
mitogen activated protein kinase PRKM13/MAPK13	602899	NM_00275 4	*****
mitogen activated protein kinase SAPK2A/MAPK14	600289	NM_00131 5	6p21.3- p21.2
vitamin D3 receptor	601769	NM_00037 6	12q12-q14
transferrin receptor	190010	NM_00323 4	3q29
thyroid stimulating hormone receptor	603372	NM_00036 9	14q31
TEK tyrosine kinase receptor (TIE-2)	600221	X60957	9p21
totipotent stem cell receptor FLK 2	600007	U03858	*****
leutenizing hormone choriogonadotropin receptor/LHCGR	152790	*****	2p21
vitamin B12 receptor/cubilin/CUBN	602997	NM_00108 1	10p12.1
neurotrophic tyrosine kinase receptor/NTRK1/TRKA	191315	X03541	1q21-q22
neurotrophic tyrosine kinase receptor/NTRK2/TRKB	600456	X75958	9q22.1
neurotrophic tyrosine kinase receptor/NTRK3/TRKC	191316	U05012	15q25
colony stimulating factor 1 receptor/CSFR1	164770	U63963	5q33.2- q33.3

Receptors

granulocyte-macrophage colony stimulating factor 2 receptor, alpha, low-affinity/CSF2RA	306250	NM_006140	Xp22.32
granulocyte-macrophage colony stimulating factor 2 receptor, beta/CSF2RB	138981	U18373	22q12.2-q13.1
granulocyte-macrophage colony stimulating factor 2 receptor, alpha, Y chromosomal/CSF2RY	425000	*****	Yp11
MTV oncogene homolog 1/AKT1	164730	K02777	14q32.3
MTV oncogene homolog 2/AKT2	164731	NM_001626	19q13.1-q13.2
erythropoietin receptor/EPOR	133171	NM_000121	19p13.3-p13.2
neutrophil chemotactic response receptor/gp130	162820	*****	7q22-qter
ciliary neurotrophic factor receptor/CNTFR	118946	NM_001842	9p13
tumor necrosis factor receptor superfamily, member 1A/TNFRSF1A	191190	NM_001065	12p13.2
tumor necrosis factor receptor superfamily, member 1B/TNFRSF1B	191191	NM_001066	1p36.3-p36.2
tumor necrosis factor receptor superfamily, member 4/TNFRSF4	600315	NM_003327	1p36
tumor necrosis factor receptor superfamily, member 5/TNFRSF5	109535	NM_001250	20q12-q13.2
tumor necrosis factor receptor superfamily, member 6B/TNFRSF6B	603361	NM_003823	20q13
tumor necrosis factor receptor superfamily, member 7/TNFRSF7	186711	*****	12p13

tumor necrosis factor receptor superfamily, member 8/TNFRSF8	153243	NM_00124 3	1p36
tumor necrosis factor receptor superfamily, member 9/TNFRSF9	602250	NM_00156 1	1p36
superfamily, member 10A/TNFRSF10A	603611	NM_00384 4	8p21
superfamily, member 10B/TNFRSF10B	603612	NM_00384 2	8p22-p21
superfamily, member 10C/TNFRSF10C	603613	AF014794	8p22-p21
superfamily, member 10D/TNFRSF10D	603614	NM_00384 0	8p21
superfamily, member 11A/TNFRSF11A	603499	NM_00383 9	18q22.1
superfamily, member 11B/TNFRSF11B	602643	NM_00254 6	8q24
tumor necrosis factor receptor superfamily, member 12/TNFRSF12	603366	NM_00379 0	1p36.3
tumor necrosis factor receptor superfamily, member 14/TNFRSF14	602746	NM_00382 0	1p36.3- p36.2
tumor necrosis factor receptor superfamily, member 16/TNFRSF16	162010	NM_00250 7	17q21-q22
tumor necrosis factor receptor superfamily, member 17/TNFRSF17	109545	Z14954	16p13.1
tumor necrosis factor receptor superfamily, member 18/TNFRSF18	603905	*****	1p36.3
proliferating cell nuclear antigen	176740	J04718	20p12
protein kinase C alpha	176960	X52479	17q22- q23.2
protein kinase C beta	176970	X06318	16p11.2

protein kinase C delta	176977	L07861	3p
protein kinase C gamma	176980	*****	19q13.4
protein kinase C theta	600448	L01087	10p15
protein kinase C zeta	176982	L14283	*****
casein kinase 1 alpha 1	600505	NM_00189 2	13q13
casein kinase 1 gamma 2	602214	U89896	19p13.3
casein kinase 1 delta	600864	NM_00189 3	17q25
casein kinase 1 epsilon	600863	NM_00189 4	22q12-q13
casein kinase 2 alpha 1	115440	J02853	20p13
casein kinase 2 alpha 2	115442	NM_00189 6	16p13.3- p13.2
casein kinase 2 beta	115441	X57152	6p21.3
mitogen-activated protein kinase kinase 1/MAP2K1	176872	NM_00275 5	15q22.1- q22.33
mitogen-activated protein kinase kinase 2/MAP2K2	601263	L11285	*****
mitogen-activated protein kinase kinase 3/MAP2K3	602315	NM_00275 6	17q11.2
mitogen-activated protein kinase kinase 4/MAP2K4	601335	NM_00301 0	17p11.2
mitogen-activated protein kinase kinase 5/MAP2K5	602520	NM_00275 7	*****
mitogen-activated protein kinase kinase 6/MAP2K6	601254	U39065	*****
mitogen-activated protein kinase kinase 7/MAP2K7	603014	NM_00504 3	*****
fos proto-oncogene/FOS	164810	K00650	14q24.3

myc proto-oncogene/MYC	190080	V00568	8q24.12-q24.13
clustrin/TRPM-2	185430	M64722	8p21-p12
c-jun	165160	J04111	1p32-p31
c-myb	189990	M15024	6q22
mdm-2	164785	Z12020	12q14.3-q15
NF kappaB	164012	*****	10q24
cAMP-dependent protein kinase/protein kinase A	176910	X14968	3p21.3-p21.2
raf-1	164760	NM_002880	3p25
H-ras	190020	J00277	11p15.5
K-ras	190070	K01912	12p12.1
N-ras	164790	X02751	1p13.2
1/WT1	194070	AH003034	11p13
neuroblastoma-derived AMV related oncogene/MYCN	164840	NM_005378	2p24.1
GRFS related oncogene/FGR	164940	NM_005417	1p36.2-p36.1
v-abl oncogene homolog 2/ABL2	164690	M14904	1q24-q25
v-abl oncogene homolog 1/ABL1	189980	U07563	9q34.1
murine sarcoma 3611-derived oncogene 1/v-RAF/ARAF1	311010	NM_001654	Xp11.4-p11.2
murine sarcoma 3611-derived oncogene 2/v-RAF/ARAF2	164710	*****	7p11.4-cen
AVE E26 oncogene homolog 1/v-ETS/ETS1	164720	NM_005239	11q23.3
AVE E26 oncogene homolog 2/v-ETS/ETS2	164740	M11922	21q22.3

teratoma oncogene TC21	600098	M31470	*****	2q14-q21
liver cancer oncogene/LCO	165320	*****		
V-FES FSV/V-FPS FASV oncogene homolog/FES	190030	NM_00200	5	15q26.1
glioma-associated oncogene homolog/GLI	165220	NM_00526	9	12q13.2-q13.3
V-CRK ASV CT10 oncogene homolog/CRK	164762	NM_00520	6	17p13.3
V-CRK ASV CT10 oncogene homolog-like/CRKL	602007	X59656		22q11
epithelial cell transforming sequence 2 oncogene/ECT2	600586	*****		3q26.1-q26.2
V-RAF MSV oncogene homolog B1/BRAF	164757	AH003899		7q34
S13 AEV oncogene homolog/SEA	165110	*****		11q13
neuroblastoma suppressor/NBS	256700	NM_00538	0	1p36.3-p36.2
hepatocyte growth factor receptor/oncogene MET/MET	164860	NM_00024	5	7q31
MOS oncogene homolog/MOS	190060	NM_00537	2	8q11
nuclear receptor coactivator/AIB1	601937	NM_00653	4	20q12
signal transducer and activator of transcription/STAT1	600555	M97935		2q32.2-q32.3
lipocortin 1/annexin 1	151690	V00546		9q11-q22
lipocortin 2/annexin 2	151740	D00017		15q21-q22
lipocortin 3/annexin 3	106490	NM_00513	9	4q21

Signaling

AVE E26 oncogene homolog related/ERG	165080	NM_004449	21q22.3
AVE E26 oncogene homolog ETS related/ELK1	311040	M25269	Xp11.2
SFFV virus-induced erythroleukemia oncogene/SP11	165170	NM_003120	11p12-p11.22
VAV oncogenem 1/AV1	164875	NM_005428	19p13.3-p13.2
VAV oncogenem 2/AV2	600428	NM_003371	9q34
ASV oncogene homolog/SRC	190090	NM_005417	20q12-q13
YSV oncogene homolog 1/YES1	164880	NM_005433	18p11.3
ASV oncogene homolog/SKI	164780	NM_003036	1q22-q24
ASV oncogene homolog-like/SKIL/SNO	165340	NM_005414	*****
lung carcinoma-derived AMV oncogene homolog 1/MYCL1	164850	M19720	1p34.3
AMV oncogene homolog 1-like/MYCL2	164865	M64786	7p15
MCF.2 cell line-derived transforming sequence/MCF2	311030	J03639	Xq27
1/THRA	190120	M24898	17q11.2
1/THRB	190160	S72623	3p24.3
cancer Osaka thyroid (COT) oncogene/COT	603259	D14497	10p11.2
CAS-BR-M murine ecotropic retroviral oncogene/CBL	165360	*****	11q23.3

lipocortin 5/annexin 5	131230	NM_00115 4	4q26-q28
lipocortin 7/annexin 7 (splice variant 1)	186360	NM_00403 4	10q21.1-q21.2
lipocortin 7/annexin 7 (splice variant 2)	186360	NM_00115 6	10q21.1-q21.2
BCL2	151430	M13994	18q21.3
BCL-X/BCLX	600039	Z23115	*****
BCL2 associated protein/BAX	600040	L22473	19q13.3-q13.4
BCL2-antagonist/killer 1/BAK1	600516	NM_00118 8	6p21.3-p21.2
BCL2-associated athanogene 1/BAG1	601497	NM_00432 3	9p12
BCL2-associated athanogene 2/BAG2	603882	NM_00428 2	*****
BCL2-associated athanogene 3/BAG3	603883	AF095193	*****
BCL2-associated athanogene 4/BAG4	603884	AF095194	*****
BCL2-associated athanogene 5/BAG5	603885	AF095195	*****
BCL-X/BCL-2 binding protein/BAD	603167	AF021792	*****
BCL2-like 1/BCL2L1	600039	NM_00119 1	*****
BCL2-like 2/BCL2L2	601931	NM_00405 0	14q11.2-q12
BCL2-like 11 (apoptosis facilitator)/BCL2L11	603827	NM_00653 8	*****
BCL2-related protein A1/BCL2A1	601056	Y09397	15q24.3
BCL2-interacting protein harikari/HRK	603447	NM_00380 6	*****
Bcl-2 interacting killer/BIK	603392	U34584	*****

apoptosis inhibitor 1/API1	601712	NM_00116 6	11q22-q23
apoptosis inhibitor 2/API2	601721	NM_00116 5	11q22-q23
apoptosis inhibitor 3/API3	300079	NM_00116 7	Xq25
apoptosis inhibitor 4/API4	603352	NM_00116 8	*****
secreted apoptosis related protein 1/SARP1/SFRP2	604157	AF017986	4q31.3
secreted apoptosis related protein 2/SARP2/SFRP1	604156	AF017987	8p12-p11.1
secreted apoptosis related protein 3/SARP3/SFRP5	604158	AF017988	10q24.1
programmed cell death 1/PDCD1	600244	NM_00501 8	2q37.3
programmed cell death 2/PDCD2	600866	NM_00259 8	6q27
programmed cell death 8/apoptosis- inducing factor/AIF/PDCD8	300169	NM_00420 8	Xq25-q26
map-kinase activating death domain/DENN	603584	U44953	11p11.2
death-associated protein/DAP	600954	NM_00439 4	5p15.2
death-associated protein kinase 1/DAPK1	600831	NM_00493 8	9q34.1
death associated protein 3/DAP3	602074	NM_00463 2	1q21
death-associated protein kinase 3/DAPK3	603289	NM_00134 8	19q13.3

death associated protein 6/DAXX/DAP6	603186	AF050179	6p21.3
defender against cell death 1/DAD1	600243	NM_00134 4	14q11-q12
BH3 interacting domain death agonist/BID	601997	NM_00119 6	22q11.2
TNF receptor-1 associated protein/TRADD	603500	L41690	16q22
CASP2 and RIPK1 domain containing adaptor with death domain/CRADD	603454	NM_00380 5	12q21.33- q23.1
neuronal apoptosis inhibitory protein/NAIP	600355	NM_00453 6	5q12.2- q13.3
RING finger protein/ROC1	603814	AF142059	*****
RING finger protein/ROC2	603863	AF142060	3q22-q24
tumor protein p53/TP53	191170	X02469	17p13.1
apoptosis linked gene/calcium binding protein/ALG2	601057	AF035606	5p15.2-pter
requiem, apoptosis response zinc finger gene/REQ	601671	NM_00626 8	11q13
Fas (TNFRSF6)-associated via death domain/FADD	602457	NM_00382 4	11q13.3
chromosome segregation 1 (yeast homolog)-like/CSE1L	601342	NM_00131 6	20q13
superfamily, member 6/FAS/TNFRSF6	134637	NM_00004 3	10q24.1
apoptotic protease activating factor/APAF1	602233	NM_00116 0	*****
receptor-interacting serine-threonine kinase 1/RIPK1	603453	NM_00380 4	*****

receptor-interacting serine-threonine kinase 2/RIPK2	603455	NM_003821	8q21
apoptosis response protein/PAPR	601936	NM_002583	12q21
apoptosis-related cysteine protease 1/caspase 1/CASP1	147678	L27475	11q22.2-q22.3
apoptosis-related cysteine protease 1/caspase 1/CASP2	600639	*****	7q35
apoptosis-related cysteine protease 1/caspase 1/CASP3	600636	NM_004346	4q35, 4q33-q35.1
apoptosis-related cysteine protease 1/caspase 1/CASP4	602664	NM_004347	11q22.2-q22.3
apoptosis-related cysteine protease 1/caspase 1/CASP5	602665	NM_004347	11q22.2-q22.3
apoptosis-related cysteine protease 1/caspase 1/CASP6	601532	NM_001226	4q25-q25
apoptosis-related cysteine protease 1/caspase 1/CASP7	601761	NM_001227	10q25.1-q25.2
apoptosis-related cysteine protease 1/caspase 1/CASP8	601763	NM_001228	2q33-q34
apoptosis-related cysteine protease 1/caspase 1/CASP9	602234	*****	*****
apoptosis-related cysteine protease 1/caspase 1/CASP10	601762	NM_001230	2q33-q34
apoptosis-related cysteine protease 1/caspase 1/CASP13	603653	NM_003723	*****

Table 2. Central Nervous System Gene List

Class	Pathway	Function	Name	OMIM	GID	Locus
-------	---------	----------	------	------	-----	-------

Concentration of Transmitter in Vesicles	vacuolar ATPase subunit I	300197	NM_001183	*****
	vacuolar ATPase subunit H	603931	NM_003945	*****
	vacuolar ATPase subunit D	603097	NM_004691	*****
	vacuolar ATPase subunit C	108745	NM_001694	16p13.3
	vacuolar ATPase subunit F	603717	*****	*****
	vacuolar ATPase subunit E	108746	NM_001696	22q11.2
	vacuolar ATPase subunit B	192132	AH007312	2cen-q13
	vacuolar ATPase subunit N	192130	NM_001991	17q21
	chromogranin A	118910	NM_001275	14q32
	chromogranin B	118920	NM_001819	20pter-p12
	chromogranin C/secretogranin 2	118930	*****	2q35-q36
	carboxypeptidase E/CPE	114855	NM_001873	Chr.4
	secretory granule neuroendocrine protein 1/SGNE1	173120	NM_003020	15q11-q15
	Nerve growth factor inducible protein/VGF	602186	NM_003378	7q22
	neuronal calcium sensor 1/NCS1/frequenin	603315	*****	*****
	amphiphysin	600418	NM_001635	7p14-p13
	synapsin 1	313440	*****	Xp11.4-p11.2
	synapsin 2	600755	*****	3p
	synapsin 3	602705	NM_003490	22q12.3
	syntaxin 1A	186590	D37932	7q11.2
	syntaxin 1B	601485	*****	16p11.2
	syntaxin 3A	600876	NM_004177	*****
	syntaxin 4A	186591	NM_004604	*****
	syntaxin 5A	603189	NM_003164	*****
	syntaxin 6	603944	NM_005819	*****
	syntaxin 7	603217	NM_003569	Chr.6
	syntaxin 10	603765	NM_003765	*****

syntaxin 16	603666	AF038897	*****
syntaxin binding protein 1	602926	NM_003165	9q34.1
syntaxin binding protein 2	601717	U63533	9p13.3-p13.2
neurexin 1	600565	AB011182	*****
neurexin 2	600566	*****	*****
neurexin 3	600567	NM_004796	*****
synaptotagmin 1/SYT1	185605	NM_005639	12cen-q21
synaptotagmin 2/SYT2	600104	*****	1q
synaptotagmin 3/SYT3	600327	*****	19q
synaptotagmin 4/SYT4	600103	*****	5q
synaptotagmin 5/SYT5	600782	*****	11p
synaptobrevin 1/VAMP1	185880	AH002992	12p
synaptobrevin 2/VAMP2	185881	AH002993	17pter-p12
cellubrevin/VAMP3	603657	*****	*****
endobrevin/VAMP8	603177	*****	*****
N-ethylmaleimide sensitive	601633	*****	17q21-q22
soluble NSF-attachment protein			
gamma/gamma SNAP	603216	NM_003826	*****
soluble NSF-attachment protein			
alpha/alpha SNAP	603215	NM_003827	*****
synaptosomal-associated protein			
23/SNAP23	602534	NM_003825	*****
synaptosomal-associated protein			
25/SNAP25	600322	NM_003081	20p11.2
Golgi SNARE 27/membrin	604027	NM_004287	17q21
Golgi SNARE 28	604026	*****	17q11
secretion deficient 22C	604028	AF039568	*****
secretion deficient 22L1	604029	NM_004892	1q21.2-q21.3
bassoon homolog	604020	NM_003458	3p21.31

Neurotransmitter Release

Packaging of Neurotransmitter into Vesicles and Release
(common to all small molecule neurotransmitters excluding nitric oxide)

voltage-dependent Ca channel L type subunit 1A	601011	NM_000068	19p13
voltage-dependent Ca channel N type subunit 1B	601012	NM_000718	9q34
voltage-dependent Ca channel L type subunit 1D	114206	NM_000720	3p14.3
large conductance Ca-activated K channel M type subunit 1B	603951	NM_004137	5q34
large conductance Ca-activated K channel M type subunit 1A	600150	U09384	Chr.10
RAS-associated protein RAB1	179508	NM_004161	2p14-p13.4
RAS-associated protein RAB2	179509	M28213	*****
RAS-associated protein RAB3A	179490	NM_002866	19p13.1-p12
RAS-associated protein RAB3B	179510	NM_002867	1p32-p31
RAS-associated protein RAB4	179511	NM_004578	1q42-q43
RAS-associated protein RAB5A	179512	NM_004162	3p24-p22
RAS-associated protein RAB6	179513	NM_002869	2q14-q21
agrin	103320	S44195	1pter-p32
synaptic vesicle protein 2/SV2	185860	*****	*****
synaptic vesicle protein 2B/SV2B	185861	*****	*****
axonal transporter of synaptic vesicles/ATSV	601255	NM_004321	2q37
synaptophysin/SVP	313475	X06389	p11.23-p11.2
phosphatidylinositol-4-kinase alpha catalytic subunit/PIK4CA	600286	NM_002650	*****
phosphatidylinositol-4-kinase beta catalytic subunit/PIK4CB	602758	NM_002651	1q21.1-q21.3
dynamitin 1/DNMI	602377	NM_004408	9q34
paired basic amino acid cleaving enzyme/furin/PACE	136950	X04329	15q25-q26

General Signal Transduction	beta 1 adaptin/ADTB1	600157	NM_001127	22q12
	beta 3A adaptin/ADTB3A	603401	NM_001284	*****
	gamma adaptin/ADTBG	603533	NM_001283	16q23
	gamma 2 adaptin/ADPTG2	603534	NM_001283	NM_001283
	human homolog of S. cerevisiae VT11	603207	AF035824	*****
	huntingtin (Huntington disease)/HD	143100	NM_002111	4p16.3
	huntingtin-associated protein 1/HAP2	600947	AF040723	17q
	phospholipase C beta 4/PLCB4	600810	NM_000933	20p12
	calmodulin 1/CALM1	114180	AH005370	14q24-q31
	calmodulin 2/CALM2	114182	NM_001743	2p21.3-p21.1
Biosynthesis	calmodulin 3/CALM3	114183	NM_005184	9q13.2-q13.3
	calcium/calmodulin dependent protein kinase II alpha/CAMK2A	114078	*****	*****
	calcium/calmodulin dependent protein kinase II gamma/CAMK2G	602123	NM_001222	10q22
	calcium/calmodulin dependent protein kinase IV/CAMK4	114080	*****	5q21-q23
	Glutaminase	138280	AB020645	2q32-q34
	Glutamate dehydrogenase 1	138130	X07674	10q23.3
	Glutamate dehydrogenase 2	300144	U08997	Xq25
	Glutamate Receptor, Ionotropic, Ampa 1; Gria1	138248	M64752	5q33
	Glutamate Receptor, Ionotropic, Ampa 2; Gria2	138247	L20814	4q32-q33
	Glutamate Receptor, Ionotropic, Ampa 3; Gria3	305915	X82068	Xq25-q26
	Glutamate Receptor, Ionotropic, Ampa 4; Gria4	138246	NM_000829	11q22-q23

Glutamate Receptor, Ionotropic, Delta 2; Grid2	602368	AF009014	4q22
Glutamate Receptor, Ionotropic, Kainate 1; Grik1	138245	U16125	21q22
Glutamate Receptor, Ionotropic, Kainate 2; Grik2	138244	S75105	6q21
Glutamate Receptor, Ionotropic, Kainate 3; Grik3	138243	U16127	1p34-p33
Glutamate Receptor, Ionotropic, Kainate 4; Grik4	600282	S67803	11q22.3
Glutamate Receptor, Ionotropic, Kainate 5; Grik5	600283	S40369	19q13.2
Glutamate Receptor, Ionotropic, N-Methyl-D-Asp 1; Grin1	138249	L13266	9q34.3
Glutamate Receptor, Ionotropic, N-Methyl-D-Asp 2a; Grin2a	138253	U09002	16p13
Glutamate Receptor, Ionotropic, N-Methyl-D-Asp 2b; Grin2b	138252	U28758	12p12
Glutamate Receptor, Ionotropic, N-Methyl-D-Asp 2c; Grin2c	138254	L76224	17q25
Glutamate Receptor, Ionotropic, N-Methyl-D-Asp 2d; Grin2d	602717	U77783	19q13.1-qter
Glutamate Receptor, Ionotropic, N-Methyl-D-Asp A; Grina	138251	*****	8q24.3
Glutamate Receptor, Metabotropic 2/G protein-coupled/ Grm2	604099	L35318	*****
Glutamate Receptor, Metabotropic 3/G protein-coupled/Grm3	601115	X77748	7q21.1-q21.2
Glutamate Receptor, Metabotropic 4/G protein-coupled/Grm4	604100	X80818	*****

Receptors

Glutamate
(NMDA)
Pathway

	Glutamate Receptor, Metabotropic 5/G protein-coupled/Grm5	604102	D28538	*****
	Glutamate Receptor, Metabotropic 6/G protein-coupled/Grm6	604096	U82083	*****
	Glutamate Receptor, Metabotropic 7/G protein-coupled/Grm7	604101	X94552	*****
	Glutamate Receptor, Metabotropic 8/G protein-coupled/Grm8	601116	U95025	7q31.3-q32.1
	Solute Carrier Family 1, Member 1; Slc1a1	133550	U08989	9p24
	Solute Carrier Family 1, Member 2; Slc1a2	600300	U03505	11p13-p12
Reuptake	Solute Carrier Family 1, Member 3; Slc1a3	600111	U03504	5p13
	Glutamine Synthetase	138290	X59834	1q31
	soluble glutamate oxaloacetate transaminase 1/GOT1	138180	NM_002079	0q24.1-q25.1
Catabolism	mitochondrial glutamate oxaloacetate transaminase 2/GOT2	138150	NM_002080	16q21
	aromatic L-Amino Acid Decarboxylase/AADC	107930	M76180	7p11
	tryptophan hydroxylase/TPH	191060	X52836	11p15.3-p14
Biosynthesis	14-3-3 protein ETA	113508	X78138	22q12
	14-3-3 protein ZETA	601288	M86400	2p25.2-p25.1
	14-3-3 protein BETA	601289	X57346	20q13.1
	14-3-3 protein SIGMA	601290	X57348	*****
	serotonin 5-HT receptors 5-HT1A, G protein-coupled	109760	X57829	5q11.2-q13

Serotonin	Receptors	serotonin 5-HT receptors 5-HT1B, G protein-coupled	182131	M81590	6q13
		serotonin 5-HT receptors 5-HT1C, G protein-coupled	312861	U49516	Xq24
		serotonin 5-HT receptors 5-HT1D, G protein-coupled	182133	M81590	1p36.3-p34.3
		serotonin 5-HT receptors 5-HT1E, G protein-coupled	182132	M91467	6q14-q15
		serotonin 5-HT receptors 5-HT1F, G protein-coupled	182134	L05597	3p12
		serotonin 5-HT receptors 5-HT2A, G protein-coupled	182135	D87030	13q14-q21
		serotonin 5-HT receptors 5-HT2B, G protein-coupled	601122	X77307	2q36.3-q37.1
		serotonin 5-HT receptors 5-HT2C, G protein-coupled	312861	U49516	Xq24
		serotonin 5-HT receptors 5-HT3, gated ion channel	182139	D49394	1q23.1-q23.2
		serotonin 5-HT receptors 5-HT4, G protein-coupled	602164	Y08756	5q31-q33
		serotonin 5-HT receptors 5-HT5a, G protein-coupled	601305	X81411	7q36.1
		serotonin 5-HT receptors 5-HT6, G protein-coupled	601109	L41147	1p36-p35
		serotonin 5-HT receptors 5-HT7, G protein-coupled	182137	L21195	10q21-q24
	Reuptake	serotonin transporter	182138	X70697	17q11.1-q12
	Catabolism	monoamine oxidase A; MAOA	309850	M69226	Xp11.23
monoamine oxidase B; MAOB		309860	M69177	Xp11.23	

		Catabolism	serotonin N-Acetyltransferase/SNAT	600950	U40347	17q25
			tryptophan 2,3-dioxygenase/TDO2	191070	NM_005651	4q31-q32
Small Molecule Neurotransmitters	Dopamine Pathway	Biosynthesis	Aromatic L-Amino Acid Decarboxylase/AADC/dopa decarboxylase	107930	M76180	7p11
			Tyrosine Hydroxylase	191290	X05290	11p15.5
		Receptors	Dopamine Receptor D1	126449	X58987	5q35.1
			Dopamine Receptor D2/DRD2	126450	NM_000795	11q23
			Dopamine Receptor D3/DRD3	126451	U32499	3q13.3
			Dopamine Receptor D4	126452	L12398	11p15.5
			Dopamine Receptor D5	126453	M67439	4p16.1-p15.3
		Reuptake	Dopamine Transporter/ DAT1	126455	L24178	5p15.3
		Catabolism	Dopamine Beta- Hydroxylase/monooxygenase	223360	Y00096	9q34
			Catechol-O-Methyltransferase	116790	M58525	22q11.2
			Monoamine Oxidases A	309850	M69226	Xp11.23
			Monoamine Oxidases B	309860	M69177	Xp11.23
			Phenol Sulfotransferase 1	171150	L10819	6p12.1-p11.2
			Phenol Sulfotransferase 2	601292	X78282	16p12.1-p11.2
			Phenol Sulfotransferase 3	600641	L19956	16p11.2
			dopamine beta hydroxylase	223360	Y00096	9q34
		Biosynthesis	phenylethanolamine-N- tyrosine Hydroxylase	171190	NM_002686	17q21-q22
			tyrosine Hydroxylase	191290	X05290	11p15.5
			alpha-1a-adrenergic receptor;	104219	M76446	Chr.20
			alpha-1b-adrenergic receptor;	104220	L31773	5q33
			alpha-1c-adrenergic receptor;	104221	D25235	8p21
			alpha-1d-adrenergic receptor;	104222	M76446	20p13
			alpha-2a-adrenergic receptor;	104210	M18415	10q24-q26
			alpha-2b-adrenergic receptor;	104260	AF005900	Chr.2

Epinephrine and Norepinephrine Pathway	Receptors	alpha-2c-adrenergic receptor;	104250	J03853	4q16.1
		beta-1-adrenergic receptor; Adrb1	109630	J03019	10q24-q26
		Beta-2-Adrenergic Receptor; Adrb2	109690	M15169	5q32-q34
		beta-adrenergic receptor kinase			
		1/BARK1	109635	NM_001619	11cen-q13
		Beta-2-Adrenergic Receptor-Like Protein G-21	109760	X57829	5q11.2-q13
		Beta-3-Adrenergic Receptor; Adrb3	109691	X70811	8p12-p11.2
		Beta-Adrenergic Receptor Kinase 1; Adrbk1	109635	X61157	11cen-q13
		Beta-Adrenergic Receptor Kinase 2; Adrbk2	109636	X69117	22q11
		Vesicular Amine Transporter 2; VAT2	193001	L09118	10q25
	Reuptake	Vesicular Amine Transporter 1; VAT1	193002	*****	8p21.3
		Solute carrier family 6, member 5/SLC6A2/NAT1/NET1	163970	NM_001043	16q12.2
	Catabolism	Monoamine Oxidase A; MAOA	309850	M69226	Xp11.23
		Monoamine Oxidase B; MAOB	309860	M69177	Xp11.23
		Catechol-O-Methyltransferase	116790	M58525	22q11.2
		Choline acetyltransferase/CHAT	118490	NM_003055	10q11.2
	Biosynthesis	carnitine acetyltransferase/CRAT	600184	NM_004003	9q34.1
		apolipoprotein E	107741	NM_000041	19q13.2
		Cholinergic Receptor, Muscarinic, 1; CHRM1	118510	X15263	11q13
		Cholinergic Receptor, Muscarinic, 2; CHRM2	118493	U19800	7q35-q36
		Cholinergic Receptor, Muscarinic, 3; CHRM3	118494	U29589	1q41-q44

Acetylcholine Pathway	Receptors	Cholinergic Receptor, Muscarinic, 4; CHRM4	118495	M16405	11p12-p11.2
		Cholinergic Receptor, Muscarinic, 5; CHRM5	118496	AF026263	15q26
		Nicotinic, Cholinergic receptor alpha 1	100690	X70108	2q24-q32
		Nicotinic, Cholinergic receptor alpha 2	118502	U62431	Chr.8
		Nicotinic, Cholinergic receptor alpha 3	118503	X53559	15q24
		Nicotinic, Cholinergic receptor alpha 4	118504	U62433	20q13.2-q13.3
		Nicotinic, Cholinergic receptor alpha 5	118505	M83712	15q24
		Nicotinic, Cholinergic receptor alpha 7/CHRNA7	118511	U40583	15q14
		Nicotinic, Cholinergic receptor beta 1	100710	X14830	17p12-p11
		Nicotinic, Cholinergic receptor beta 2	118507	Y08415	1p21
	Reuptake	Nicotinic, Cholinergic receptor beta 3	118508	X67513	8p11.2
		Nicotinic, Cholinergic receptor beta 4	118509	X68275	15q24
		Nicotinic, Cholinergic receptor epsilon polypeptide	100725	X66403	Chr.17
		Nicotinic, Cholinergic receptor,	100720	X55019	2q33-q34
		Nicotinic, Cholinergic receptor,	100730	NM_005199	2q33-q34
		Vesicular acetylcholine transporter	600336	NM_003055	10q11.2
	Catabolism	Acetylcholinesterase/ACHE	100740	M55040	7q22
		butyrylcholinesterase 1/serum cholinesterase 1/BCHE1	177400	NM_000055	3q26.1-q26.2
		butyrylcholinesterase 2/serum cholinesterase 2/BCHE2	177500	*****	2q33-q35
		Histidine Decarboxylase	142704	M60445	15q21-q22
Biosynthesis	Receptors	histamine H1 receptor/HRH1	600167	NM_000861	3p21-p14
		histamine H2 receptor/HRH2	142703	AB023486	*****

Histaminergic Pathway	histamine H3 receptor/HRH3	*****	NM_00723 2	*****
		*****	NM_006895	chr. 2
Catabolism	Histamine N-			
	Amine oxidase (copper-containing) 2/AOC2	602268	D88213	17q21
	Amine oxidase (copper-containing) 3/AOC3	603735	AF054985	17q21
Biosynthesis	adenylosuccinate lyase/ADSL	103050	NM_000026	22q13.1
	adenylosuccinate synthetase/ADSS	103060	NM_001126	1cen-q12
	Adenosine A1 Receptor; Adora1/G protein-coupled	102775	L22214	1q32.1
Receptors	Adenosine A2 Receptor; Adora2a/G protein-coupled	102776	X68486	22q11.2
	Adenosine A2b Receptor; Adora2b/G protein-coupled	600446	X68487	17p12-p11.2
	Adenosine A3 Receptor; Adora3/G protein-coupled	600445	L20463	1p21-p13
	Adenosine A2 Receptor- like/ADORA2L1	102777	*****	10q25.3-q26.1
	Purinergic Receptor P2x, Ligand- Gated Ion Channel, 1; P2rx1	600845	NM_002558	*****
	Purinergic Receptor P2x, Ligand- Gated Ion Channel, 3; P2rx3	600843	Y07683	11q12
	Purinergic Receptor P2x, Ligand- Gated Ion Channel, 4; P2rx4	600846	AF000234	12q24.32
	Purinergic Receptor P2x, Ligand- Gated Ion Channel, 5; P2rx5	602836	NM_002561	*****
	Purinergic Receptor P2x, Ligand- Gated Ion Channel, 7; P2rx7	602566	Y09561	12q24
Adenosine Pathway				

	P2Y11 purinoceptor/G protein-receptor/G protein-coupled	602697	*****	*****
	P2Y7 purinoceptor/leukotriene B4 receptor/G protein-coupled	601531	NM_000752	14q11.2-q12
	P2Y2 purinoceptor/G protein-coupled	600041	U07225	1q13.5-q14.1
	P2Y1 purinoceptor/G protein-coupled	601167	U42029	3q25
	P2Y4 pyrimidinergic receptor/G protein-coupled	300038	NM_002565	Xq13
	P2Y6 pyrimidinergic receptor/purinoreceptor P2Y6/G protein-coupled/P2RY6	602451	NM_004154	11q13.5
Reuptake	Solute carrier family 29 (nucleosides), member 1/SLC29A1/ENT1	602193	NM_004955	6p21.2-p21.1
	Solute carrier family 29 (nucleosides), member 2/SLC29A2/ENT2	602110	X86681	11q13
Catabolism	adenosine deaminase	102700	NM_000022	20q13.11
Biosynthesis	Glutamate decarboxylase 1 (brain, 67kD)	266100	M81883	2q31
	Glutamate decarboxylase 2 (brain, 65kD)	138275	X69936	10p11.23
	Glutamate decarboxylase 3	138276	138276	22q13
	Gamma-Aminobutyric Acid Receptor, Beta-3; Gabrb3	137192	M82919	15q11.2-q12
	Gamma-Aminobutyric Acid Receptor, Alpha-3; Gabra3	305660	S62908	Xq28
	Gamma-Aminobutyric Acid Receptor, Alpha-5; Gabra5	137142	L08485	15q11.2-q12
	Gamma-Aminobutyric Acid Receptor, Alpha-1; Gabral	137160	X14766	5q34-q35

Gamma-Aminobutyric Acid Receptor, Alpha-6; Gabra6	137143	S81944	5q31.1-q35
Gamma-Aminobutyric Acid B Receptor 1; Gabbr1	603540	Y11044	*****
Gamma-Aminobutyric Acid Receptor, Alpha-2; Gabra2	137140	S62907	4p13-p12
Gamma-Aminobutyric Acid Receptor, Gamma-3; Gabrg3	600233	NM_000816	15q11.2-q12
Gamma-Aminobutyric Acid Receptor, Beta-1; Gabrb1	137190	X14767	4p13-p12
Gamma-Aminobutyric Acid Receptor, Pi; Gabrp	602729	U95367	*****
Gamma-Aminobutyric Acid Receptor, Epsilon; Gabre	300093	Y09765	Xq28
Gamma-Aminobutyric Acid Receptor, Alpha-4; Gabra4	137141	U30461	4p14-q12
Gamma-Aminobutyric Acid Receptor, Beta-2; Gabrb2	600232	S77553	5q34-q35
Gamma-Aminobutyric Acid Receptor, Gamma-2; Gabrg2	137164	X15376	5q31.1-q33.1
Gamma-Aminobutyric Acid Receptor, Gamma-1; Gabrg1	137166	*****	4p14-q21.1
Gamma-Aminobutyric Acid Receptor, Delta; Gabrd	137163	AF016917	1p
Gamma-Aminobutyric Acid Receptor Subunit Rho1	137161	M62400	6q14-q21
Gamma-Aminobutyric Acid Receptor Subunit Rho2	137162	M86868	6q14-q21
Benzodiazepine receptor, peripheral	109610	NM_000714	22q13.31
diazepam binding inhibitor/DBI	125950	M15887	2q12-q21

Receptors

Gamma-Aminobutyric Acid Pathway

	Reuptake	Solute carrier family 6 (GABA), member 1/SLC6A1	137165	X54673	3p25-p24
		Solute carrier family 1, member 6 (GABA/GLU)/SLC1A6	600637	NM_005071	*****
		Solute carrier family 6 (betaine/GABA), member 12	603080	U27699	12p13
		GABA-glutamate transaminase	137150	NM_000663	*****
	Catabolism	succinic semialdehyde dehydrogenase/SSADH	271980	NM_001080	6p22
		Sacrosine dehydrogenase	268900	*****	9q33-q34
		Alanine-glyoxylate aminotransferase, cytosolic serine	259900	NM_000030	2q36-q37
		hydroxymethyltransferase 1/SHMT1 mitochondrial serine	182144	NM_004169	17p11.2
	Biosynthesis	hydroxymethyltransferase 2/SHMT2	138450	*****	12q13
		Glycine Receptor, Alpha-1 Subunit; Glra1	138491	X52009	5q32
		Glycine Receptor, Alpha-2 Subunit; Glra2	305990	X52008	Xp22.1-p21.2
		Glycine Receptor, Alpha-3 Subunit; Glra3	600421	AF018157	4q33-q34
Glycine Pathway	Receptors	Glycine Receptor, Beta Subunit; Glrb	138492	U33267	4q31.3
		Solute carrier family 6, Member 9; SLC6A9 (glycine)	601019	S70612	1p33
		Solute carrier family 6, Member 5; SLC6A5 (glycine)	604159	NM_004211	*****
		Glycine aminotransferase/glycine cleavage T protein/GAT	238310	NM_000481	3p21.2-p21.1

	Catabolism	Glycine dehydrogenase/glycine cleavage P protein	238300	M63635	9p22
		Aminomethyl carrier/glycine cleavage H protein	238330	NM_004483	*****
		Dihydroliipoamide dehydrogenase/glycine cleavage L	238331	*****	*****
Taurine	Biosynthesis	cysteine dioxygenase, type I/CDO1	603943	NM_001801	5q22-q23
		sulfite oxidase/SUOX	272300	NM_000456	*****
Melatonin	Receptors	solute carrier family 6, member 6/taurine transporter/SLC6A6	186854	U16120	3p25-q24
		serotonin N-Acetyltransferase/SNAT	600950	U40347	17q25
	Biosynthesis	X-chromosomal acetylserotonin N-methyltransferase/ASMT	300015	NM_004043	Xpter-p22.32
		Y-chromosomal acetylserotonin N-methyltransferase/ASMT	402500	*****	Ypter-p11.2
		acetylserotonin N-methyltransferase-like/ASMTL	300162	NM_004192	Xpter-p22.32
		melatonin receptor 1A/MTNR1A	600665	NM_005958	4q35.1
	Receptors	melatonin receptor 1B/MTNR1B	600804	NM_005959	11q21-q22
		tryptophan 2,3-dioxygenase/TDO2	191070	NM_005651	4q31-q32
	Catabolism	nitric oxide synthetase 1/NOS1	163731	AH001515	2q24.2-q24.3
		nitric oxide synthetase 2A/NOS2A	163730	X85766	17cen-q11.2
Nitric Oxide Pathway	Biosynthesis	macrophage nitric oxide synthetase 2B/NOS2B	600719	AH006623	17p13.1-q25
		macrophage nitric oxide synthetase 2C/NOS2C	600720	600720	17p13.1-q25
		nitric oxide synthetase 3/NOS3	163729	AH001515	7q36
		chondrocyte nitric oxide synthetase 3/NOS4	163728	X73029	*****

		arginase/ARG1	207800	NM_000045	*****
		arginase/ARG2	107830	NM_001172	4q24.1-q24.2
		membrane metalloendopeptidase/MME/neutral endopeptidase	120520	AH002677	3q21-q27
		calpain, large polypeptide L3/CAPN3	114240	NM_000070	5q15.1-q21.1
		Leucyl/cystinyl aminopeptidase	151300	U62768	*****
		carboxypeptidase N polypeptide 1/CPN1	603103	NM_001308	chr. 10
		carboxypeptidase N polypeptide 2/regulatory subunit/CPN2	603104	J05158	8p23-p22
		meprin alpha subunit/MEP1A	600388	NM_005925	6p21.2-p21.1
		meprin beta subunit/MEP1B	600389	NM_005925	8q12.2-q12.3
		prolyl endopeptidase/PREP	600400	NM_002726	6q22
		neuroendocrine convertase 1/NEC1	162150	D73407	5q14-q21
		peptidylglycine alpha-amidating monooxygenase /PAM/NEC2	170270	NM_000919	5q14-q21
		paired basic amino acid cleaving enzyme/PACE/FUR	136950	X04329	15q25-q26
		proopiomelanocortin	176830	NM_000939	2p23.3
		prepronociceptin/nociceptin/hosistatin/PNOC	601459	*****	8p21
		preproenkephalin			
		B/prodynorphin/PDYN	131340	NM_006211	12p12.21
		preproenkephalin			
		A/proenkephalin/PENK	131330	NM_006211	8q23-q24
		Opioid Receptor, Mu-1; Oprm1	600018	NM_000914	6q24-q25
		Opioid Receptor, Kappa-1; Oprk1	165196	U17298	8q11.2

	Receptors	opioid receptor-like 1/OPRL 1	602548	X77130	*****
		Opioid Receptor, Delta-1; Oprd1	165195	U10504	1p36.1-p34.3
		Opioid Receptor, Sigma 1	601978	U75283	*****
		opioid binding cell adhesion molecule/OBCAM	600632	*****	Chr.11
		G protein-coupled receptor 7/GPR7	600730	U22491	0q11.2-q21.1
Oxytocin	Biosynthesis	G protein-coupled receptor 8/GPR8	600731	U22492	20q13.3
		Oxytocin	167050	M25650	20p13
		Oxytocin receptor	167055	X64878	3p26.2
		Leucyl/cystinyl aminopeptidase	151300	U62768	*****
		Cholecystokinin/CCK	118440	L00354	3pter-p21
Cholecystokinin (CCK)	Biosynthesis	Cholecystokinin A receptor/CCKAR	118444	L13605	4p15.2-p15.1
		Cholecystokinin B receptor/CCKBR	118445	L08112	1p15.5-p15.4
		Neuropeptide Y/NPY	162640	K01911	7p15.1
		Neuropeptide Y receptor Y1/NPY1R	162641	M84755	4q31.3-q32
		Neuropeptide Y receptor Y2/NPY2R	162642	U32500	4q31
Neuropeptide Y (NPY)	Receptors	Neuropeptide Y receptor Y3/chemokine receptor 4/CXCR4	162643	X71635	2q21
		Neuropeptide Y receptor Y5	602001	U94320	4q31-q32
		Neuropeptide Y receptor Y6	601770	D86519	5q31
		leptin/LEP	164160	NM_000230	7q31.3
		leptin receptor/LEPR	601007	NM_002303	1p31
Leptin	Biosynthesis	Neurotensin	162650	U91618	12q21
		prolyl endopeptidase/PREP	600400	NM_002726	6q22
		Neurotensin receptor	162651	X70070	20q13
		Neurokinin A/Tachykinin 1 or 2/Substance P or K	162320	U37529	7q21-q22
		Neurokinin B/Tachykinin 3	162330	*****	12q13-q21
Neurotensin Pathway	Receptors				
Tachykinin or Substance P	Biosynthesis				

Neurokinin Pathway	Receptors	Tachykinin NK1 receptor/TACR1	162323	M81797	Chr.2
		Tachykinin NK2 receptor/TACR2	162321	M57414	10q11-q21
		Tachykinin NK3 receptor/TACR3	162332	M89473	*****
	Biosynthesis	kininogen/KNG	228960	*****	3q27
Bradykinin		kallikrein 1/KLK1	147910	AH002853	9q13.2-q13.4
	Receptor	bradykinin receptor B1/BDKRB1 G protein-coupled	600337	NM_000710	4q32.1-q32.2
		bradykinin receptor B2/BDKRB2 G protein-coupled	113503	NM_000623	4q32.1-q32.2
		angiotensinogen	106150	NM_000029	1q42-q43
Angiotensin	Biosynthesis	renin/REN	179820	NM_000537	1q32
		renin-binding protein/RENBP	312420	D10711	Xq28
		angiotensin converting enzyme/dipeptidyl carboxypeptidase	106180	NM_000789	17q23
	Receptors	angiotensin receptor 1/AGTR1A	106165	M87290	3q21-q25
Vasopressin		angiotensin II receptor type 2/AGTR2	300034	U10273	Xq22-q23
		vascular angiotensin II receptor type 1B/AGTR1B	600015	NM_004835	*****
	Catabolism	prolylcarboxypeptidase/PRCP	176785	NM_005040	11q14
	Biosynthesis	Arginine Vasopressin	192340	X03172	20p13
Vasopressin	Receptors	Arginine Vasopressin Receptor 1A/AVPR1A	600821	AF030625	12q14-q15
		Arginine Vasopressin Receptor 1B/AVPR1B	600264	AF030512	1q32
		Arginine vasopressin receptor 2	304800	AF030626	Xq28
	Catabolism	Leucyl/cystinyl aminopeptidase	151300	U62768	*****
Biosynthesis		prepro-vasoactive intestinal adenylate-cyclase activating polypeptide 1/ADCYAP1	192320	AH003029	6q26-q27
			102980	NM_001117	18p11

Peptide Hormones	Vasoactive Intestinal Peptide	Receptor	vasoactive intestinal peptide receptor 1/VIPR1	192321	*****	3p22
			vasoactive intestinal peptide receptor 2/VIPR2	601970	L40764	7q36.3
			adenylate-cyclase activating polypeptide 1 receptor/ADCYAP1R1	102981	D17516	7p14
		Biosynthesis	calcitonin/calcitonin gene-related peptide	114130	M12667	1p15.2-p15.1
Calcitonin and CGRP			calcitonin/calcitonin gene-related peptide	114160	X02404	1p15.2-p15.2
		Receptor	calcitonin receptor/CALCR	114131	L00587	7q21.3
			calcitonin receptor-like/CALCRL	114190	NM_005795	*****
		Biosynthesis	Corticotropin releasing hormone/CRH	122560	NM_000756	8q13
CRH			urocortin/UCN	600945	NM_003353	Chr.2
			urocortin 2/UCN2	604097	AF104118	*****
		Receptors	Corticotropin releasing hormone receptor 1	122561	U16273	17q12-q22
			Corticotropin releasing hormone receptor 2	602034	NM_001883	7p21-p15
TRH		Biosynthesis	Corticotropin releasing hormone-binding protein	122559	X58022	5q11.2-q13.3
			thyrotropin releasing hormone/TRH	275120	AH001523	3p
		Receptors	thyrotropin releasing hormone receptor/G protein coupled/TRHR	188545	X75071	8q23
		Biosynthesis	chorionic gonadotropin alpha chain/TSHA/CGA	118850	NM_000735	6q21.1-q23
TSH			thyroid stimulating hormone beta	188540	AH001548	1p13
		Receptor	thyroid stimulating hormone receptor	603372	NM_000369	14q31
			gonadotropin releasing hormone	152760	NM_000825	8p21-p11.2
		Biosynthesis	1/LHRH/GNRH1			

GRH	Biosynthesis	gonadotropin releasing hormone 2/LHRH/GNRH2	602352	NM_001501	20p13
	Receptor	gonadotropin releasing hormone receptor/G protein- coupled/LHRH/GNRHR	138850	NM_000406	4q21.2
FSH	Biosynthesis	follicle stimulating hormone- inhibin, beta A (activin A, activin AB alpha polypeptide)/INHBA	136530	AH002701	11p13
		activin A receptor, type I/ACVR1	147290	NM_002192	7p15-p13
		activin A receptor, type IB/ACVR1B	102576	NM_001105	2q23-q24
		activin A receptor type II-like 1/ACVRL1	601300	NM_004302	12q13
		activin typeII A receptor/ACVR2	601284	NM_000020	12q11-q14
		activin A receptor, type IIB/ACVR2B	102581	D31770	*****
		alpha-inhibin/INHA	602730	NM_001106	3p22-p21.3
		beta-B inhibin/beta C inhibin//INHBC	147380	M13144	2q33-q36
		follicle stimulating hormone receptor/FSHR	601233	M13437	12q13.1
		FSH primary response (LRPR1, rat) homolog 1/FSHPRH1	136435	NM_000145	2p21-p16
Somatostatin	Receptor	Somatostatin preprocartistatin	300065	NM_006733	Xq22
			182450	J00306	3q28
	Biosynthesis	Somatostatin receptor 1/G protein- coupled	602784	NM_001302	1p36
		Somatostatin receptor 2	182451	M81829	14q13
		Somatostatin receptor 3/adenyl cyclase coupled	182452	M81830	17q24
		Somatostatin receptor 4	182453	M96738	22q13.1
		Somatostatin receptor 5	182454	L07833	20p11.2
			182455	D16827	16p13.3

GHRH	Biosynthesis	growth hormone releasing hormone/GHRH	139190	AH002712	20q11.2
	Receptor	growth hormone releasing hormone receptor/G protein-coupled/GHRHR	139191	U34195	7p15-p14
Growth Hormone	Biosynthesis	growth hormone 1/somatotropin/GH1	139250	NM_000515	17q22-q24
	Receptor	growth hormone receptor/GHR	600946	NM_000163	5p13-p12
ACTH	Biosynthesis	proopiomelanocortin	176830	NM_000939	2p23.3
	Receptor	melanocortin 2 receptor/ACTH receptor/MC2R	202200	NM_000529	18p11.2
Prolactin	Biosynthesis	prolactin/PRL	176760	NM_000948	6p22.2-p21.3
	Receptor	prolactin receptor/PRLR	176761	NM_000949	5p13-p12
Galanin	Biosynthesis	preprogalanin/GAL1	137035	L11144	1q13.3-q13.5
	Receptor	galanin receptor 1 (brain)/GALR1	600377	NM_001480	18q23
	Receptor	galanin receptor 2/GALR2	603691	NM_003857	17q25.3
		galanin receptor 3 (brain)/GALR3	603692	NM_003614	2q12.2-q13.1
Bombesin	Biosynthesis	gastrin-releasing polypeptide/bombesin/GRP	137260	NM_002091	18q21
		neuromedin B/NMB	162340	M21551	15q22-qter
	Receptor	gastrin-releasing polypeptide receptor/G protein-coupled/GRPR	305670	D87058	Xp22.3-p21.2
		neuromedin B receptor/g protein-coupled/NMBR	162341	*****	6q21-qter
Glucagon Pathway		bombesin-like receptor 3/BRS3	300107	NM_001727	Xq26-q28
	Biosynthesis	preproglucagon/GCG	138030	X03991	2q36-q37
	Receptor	glucagon receptor/GCGR	138033	NM_000160	17q25
		glucagon-like peptide 1	138032	U01156	6p21
		glucagon-like peptide 2	603659	*****	17p13.3
		carbamoyl synthase (6.3.2.11)	*****	*****	*****

Carnosine Pathway	Biosynthesis	homocarnosine synthase	*****	*****	*****	*****	
		Receptor	carnosine receptor	*****	*****	*****	*****
Steroid Hormones	Estrogen	Catabolism	carnosinase/Xaa-his dipeptidase (3.4.13.3)	*****	*****	*****	*****
		Biosynthesis	cytochrome P450, subfamily XIX (androgen aromatase)/CYP19	107910	NM_000103	15q21.1	
		Receptors	estrogen receptor 1 (ESR1)	133430	M12674	6q25.1	
			estrogen receptor 2 (ESR2)	601663	X99101	14q	
			estrogen-related receptor	601998	NM_004451	11q12	
	estrogen-related receptor beta/ESRRB		602167	NM_004452	14q24.3		
	Catabolism	estrogen-preferring	600043	NM_005420	4q13.1		
	Testosterone /DHT		steroid 5-alpha-reductase 1/SRD5A1	184753	AH003000	5p15	
			steroid 5-alpha-reductase 2/SRD5A2	264600	NM_000348	2p23	
		Biosynthesis	aldo-keto reductase family 1, member C4/3-a hydroxysteroid dehydrogenase/AKR1C4	600451	*****	10p15-p14	
Receptors		androgen receptor	313700	M20132	Xq11-q12		
Catabolism		UDP glycosyltransferase 2 family, polypeptide B17/UGT2B17	601903	NM_001077	4q13		
Glucocortico steroid	Biosynthesis	cytochrome P450, subfamily XXI (steroid 21-a-hydroxylase)/CYP21	201910	M13936	6p21.3		
		cytochrome P450, subfamily XIB, polypeptide 2 (steroid 11-b-hydroxylase)/CYP11B2	124080	NM_000498	8q21		
		Receptors	glucocorticoid receptor/GRL	138040	NM_000176	5q31	
		Metabolism	corticosteroid binding globulin precursor/CBG	122500	NM_001756	14q32.1	
			hydroxy-D-5-steroid dehydrogenase, 3b- and steroid D-isomerase 2/HSD3B2	201810	NM_000198	1p13.1	

Calcium Channels	voltage-dependent calcium channel, P/Q type, alpha 1A	601011	NM_000068	19p13
	calcium channel, voltage-dependent, L type, alpha 1B subunit/CACNA1B	601012	NM_000718	9q34
	calcium channel, voltage-dependent, L type, alpha 1C subunit/CACNA1C	114205	NM_000719	12p13.3
	calcium channel, voltage-dependent, L type, alpha 1D subunit/CACNA1D	114206	NM_000720	3p14.3
	L-type voltage dependent calcium channel alpha 1S subunit/CACNA1S	114208	NM_000069	1q32
	calcium channel, voltage-dependent, beta 1 subunit/CACNB1	114207	NM_000723	17q21-q22
	voltage dependent calcium channel beta 2 subunit/CACNB2	600003	U07139	10p12
	voltage dependent calcium channel beta 3 subunit/CACNB3	601958	NM_000725	12q13
	voltage dependent calcium channel beta 4 subunit/CACNB4	601949	*****	2q22-q23
	calcium channel, voltage-dependent, alpha 2/delta subunit/CACNA2D1	114204	Z28613	7q21-q22
	calcium channel, voltage-dependent, gamma subunit/CACNG	114209	NM_000727	17q24
	neuronal voltage dependent calcium channel gamma subunit/CACNG2	602911	NM_006078	*****
	ATPase, Ca++ transporting, plasma membrane 1/ATP2B1	108731	NM_001682	12q21-q23
	ATPase, Ca++ transporting, plasma membrane 2/ATP2B2	108733	NM_001683	3p26-p25
	ATPase, Ca++ transporting, plasma membrane 3/ATP2B3	300014	AF060497	Xq28

ATPase, Ca++ transporting, plasma membrane 4/ATP2B4	108732	NM_001684	1q25-q32
	180901	AH006668	19q13.1
gene/RYR1	170500	U24693	7q23.1-q25.3
sodium channel alpha-subunit/SCN4A	182390	M94055	2q23-q24.3
type II voltage dependent sodium channel alpha 1 subunit/SCN2A1	603415	NM_002977	2q24
type IX voltage dependent sodium channel alpha subunit/SCN9A	182389	S71446	2q24
type I voltage dependent sodium channel alpha subunit/SCN1A	182391	S69887	2q24
type III voltage dependent sodium channel alpha subunit/SCN3A	601327	NM_004588	11q22-qter
type II voltage dependent sodium channel beta subunit/SCN2B	182392	M55662	2q21-q23
type VI voltage dependent sodium channel alpha subunit/SCN6A	603967	NM_000334	7q23.1-q25.3
type IV voltage dependent sodium channel alpha subunit/SCN4A	600163	NM_000335	3p24-p21
type V voltage dependent sodium channel alpha subunit/SCN5A	600702	*****	12q13
type VIII voltage dependent sodium channel alpha subunit/SCN8A	601219	M55662	2q23-q24
type II voltage dependent sodium channel alpha 2 subunit/SCN2A2	600235	NM_001037	19q13.1
type I voltage dependent sodium channel beta subunit/SCN1B	601784	NM_001094	17q11.2-q12
voltage independent neuronal sodium channel 1/ACCN1			

Sodium Channels

Channels

Potassium Channels	voltage independent neuronal sodium channel 2/ACCN2	602866	NM_001095	12q12
	cyclic nucleotide gated hyperpolarization activated potassium	602780	AF064876	*****
	cyclic nucleotide gated hyperpolarization activated potassium	602781	AF064877	*****
	voltage dependent potassium channel, KQT-like subfamily, member	602235	NM_000218	20q13.3
	voltage dependent potassium channel, KQT-like subfamily, member	602232	AF033347	8q24
	voltage dependent potassium channel, subfamily F, member 1/KCNF1	603787	NM_002236	2p25
	voltage dependent potassium channel, subfamily H, member 1/KCNH2	603305	NM_002238	1q32-q41
	inwardly rectifying potassium channel, subfamily J, member 4/KCNJ4	600504	NM_004981	22q13.1
	inwardly rectifying potassium channel, subfamily J, member 14/KCNJ14	603953	*****	*****
	inwardly rectifying potassium channel, subfamily J, member 2/KCNJ3/HHIRK1	600681	NM_000891	*****
	inwardly rectifying potassium channel, subfamily J, member 10/KCNJ10	602208	*****	1q
	potassium channel, subfamily J, member 13/KCNJ13	603208	AJ007557	2q37
	voltage dependent potassium channel, subfamily K, member 1/KCNK1	601745	NM_002245	1q42-q43
	voltage dependent potassium channel, subfamily K, member 2/KCNK2	603219	*****	1q41

	voltage dependent potassium channel, subfamily K, member 3/KCNK3	603220	NM_002246	2p23
	G protein coupled potassium channel, subfamily J, member	601534	NM_002239	2q24.1
	G protein coupled potassium channel inward rectifier/GIRK3	600932	*****	1q21-q23
	voltage dependent potassium channel, subfamily S, member 1/KCNS1	602905	*****	*****
	voltage dependent potassium channel, subfamily S, member 2/KCNS2	602906	*****	8q22
	voltage dependent potassium channel, subfamily S, member 3/KCNK3	603888	AF043472	2p24
	large conductance Ca-activated K channel M type subunit 1B	603951	NM_004137	5q34
	large conductance Ca-activated K channel M type subunit 1A	600150	U09384	Chr.10
	chloride channel, calcium activated, family member 1/CLCA1	603906	NM_001285	1p31-p22
	chloride channel, calcium activated, family member 2/CLCA2	604003	NM_006536	*****
Chloride	chloride channel 1, skeletal muscle/CLCN1	118425	NM_000083	7q35
	chloride channel 2/CLCN2	600570	NM_004366	3q26-qter
	chloride channel 3/CLCN3	600580	NM_001829	4q33
	chloride channel 4/CLCN4	302910	NM_001830	Xp22.3
	chloride channel 5/CLCN5	300008	NM_000084	Xp11.22
	chloride channel 6/CLCN6	602726	NM_001286	1p36
	phospholipase A2 group	172411	NM_000300	1p35
	phospholipase A2 group IB/PLA2G1B	172410	NM_000928	12q23-q24.1

Prostaglandins	Biosynthesis	phospholipase A2 group X/PLA2G10	603603	*****	16p13.1-p12
		phospholipase A2 group IV A/PLA2G4A	600522	U08374	1q25
		phospholipase A2 group VI/PLA2G6	603604	AF064594	22q13.1
		phospholipase A2 group IVC/PLA2G4C	603602	*****	chr. 19
		phospholipase A2 group V/PLA2G5	601192	NM_000929	1p36-p34
		phospholipase C beta 3	600230	U26425	11q13
		lysosomal acid lipase	278000	NM_000235	10q24-q25
		prostaglandin endoperoxide synthetase 1/COX1/PTGS1	176805	AH001520	9q32-q33.3
		prostaglandin endoperoxide synthetase 2/COX2/PTGS2	600262	NM_000963	1q25.2-q25.3
		thromboxane A synthase 1/TBXAS1	274180	EG_D34613	7q34
		prostaglandin D2 synthase	602598	M61900	*****
		prostaglandin I2 synthase/prostacyclin synthase/PTGIS	601699	EG_D83393	20q13
	Receptors	prostaglandin E receptor 1, EP1 subtype/PTGER1	176802	NM_000955	19p13.1
		prostaglandin E receptor 2, EP2 subtype/PTGER2	176804	*****	5p13.1
		prostaglandin E receptor 3, EP3 subtype/PTGER3	176806	NM_000957	1p31.2
		prostaglandin E receptor 4, EP4 subtype/PTGER4	601586	NM_000958	5p13.1
		prostaglandin F receptor/PTGFR	600563	L24470	1p31.1
		prostaglandin F2 receptor negative regulator/PTGFRN	601204	U26664	1p13.1-q21.3
		prostaglandin I2 receptor/PTGIR/prostacyclin receptor	600022	SEG_HUMI	19q13.3

		Inflammation (additional genes in Immunology)	Platelet Activating Factor	Catabolism	15-hydroxyprostaglandin dehydrogenase/HPGD	601688	NM_000860	4q34-q35
					aldo-keto reductase family 1, member C2/AKR1C2	600450	NM_001353	10p15-p14
				Biosynthesis	CDP-choline:alkylacetyl glycerol cholinephosphotransferase	*****	*****	*****
					phospholipase A2 group	172411	NM_000300	1p35
					phospholipase A2 group IB/PLA2G1B	172410	NM_000928	12q23-q24.1
					phospholipase A2 group X/PLA2G10	603603	*****	16p13.1-p12
					phospholipase A2 group IVA/PLA2G4A	600522	U08374	1q25
					phospholipase A2 group VI/PLA2G6	603604	AF064594	22q13.1
					phospholipase A2 group IVC/PLA2G4C	603602	*****	chr. 19
					phospholipase A2 group V/PLA2G5	601192	NM_000929	1p36-p34
					platelet activating factor receptor/PTAFR	173393	M88177	1p35-p34.3
					platelet activating factor acetylhydrolase 1/PAFAH1	601690	NM_005084	6p21.2-p12
				Catabolism	platelet activating factor acetylhydrolase, isoform 1B, alpha	601545	NM_000430	17p13.3
					platelet activating factor acetylhydrolase, isoform 1B, beta	602508	NM_002572	11q23
					platelet activating factor acetylhydrolase, isoform 1B, gamma	603074	NM_002573	19q13.1
					platelet activating factor acetylhydrolase 2/PAFAH2	602344	NM_000437	*****
					interferon alpha1 (IFNa1)	147660	X02956	9p22
					interferon alpha2 (IFNa2)	147562	*****	9p22

Interferon	interferon beta1 (IFNb1)	147640	V00546	9p21
	interferon beta3 (IFNb3)	147860	*****	Chr.8
	interferon omegal (IFNw1)	147553	X02669	9p21
	interferon gamma (IFNg)	147570	L07633	12q14
	interferon alpha receptor 1 (IFNAR1)	107450	X77722	21q22.1
	interferon alpha receptor 2 (IFNAR2)	147569	U68755	21q22.1-q22.2
	interferon gamma receptor 1	107470	J03143	6q23-q24
	interferon gamma receptor 2	602376	NM_000874	21q22.1
	2',5'-oligoadenylate synthetase	164350	NM_006187	12q24.2
	2',5'-oligoadenylate synthetase	603350	M87284	12q24.2
Interleukins	2',5'-oligoadenylate synthetase	603351	*****	12q24.2
	interleukin 1 alpha/IL1A	147760	M15329	2q14
	interleukin 1 beta/IL1B	147720	K02770	2q14
	interleukin 1 receptor, type 1/IL1R1	147810	M27492	2q12
	interleukin 1 receptor, type 2/IL1R2	147811	NM_004633	2q12-q22
	interleukin 8/IL8	146930	M26383	4q12-q13
	interleukin 8 receptor alpha/IL8R1	146929	M68932	2q35
	interleukin 8 receptor beta/IL8R2	146928	M94582	2q35
	interleukin 10/IL10	124092	M57627	1q31-q32
	interleukin 10 receptor alpha/IL101	146933	U00672	11q23.3
	tumor necrosis factor alpha/TNFA	191160	X01394	6p21.3
	tumor necrosis factor			
	beta/TNFB/lymphotoxin alpha/LTA	153440	NM_000595	6p21.3
	tumor necrosis factor receptor			
	superfamily, member 1A/TNFRSF1A	191190	NM_001065	12p13.2
	tumor necrosis factor receptor			
	superfamily, member 1B/TNFRSF1B	191191	NM_001066	12p13.2
MIF	macrophage migration inhibitory factor (glycosylation-inhibiting			
		153620	NM_002415	22q11.2

Cytokines

Cardiovascular or (additional genes in Cardiovascular or and	Clotting	Clotting	factor I/fibrinogen a, alpha/FGA	134820	NM_000508	4q28
			factor I/fibrinogen b, beta/FGB	134830	AH003492	4q28
Cardiovascular or (additional genes in Cardiovascular or and	Clotting	Clotting	factor I/fibrinogen g, gamma/FGG	134850	NM_000509	4q28
			factor II/prothrombin	176930	F2	11p11-q12
Cardiovascular or (additional genes in Cardiovascular or and	Clotting	Clotting	factor III/thromboplastin	134390	NM_001993	1p22-p21
			factor V/proaccelerin/labile factor	227400	NM_000130	1q23
Cardiovascular or (additional genes in Cardiovascular or and	Clotting	Clotting	factor VII/serum prothrombin conversion accelerator	227500	NM_000131	13q34
			factor VIII/antihemophilic factor	306700	NM_000132	Xq28
Cardiovascular or (additional genes in Cardiovascular or and	Clotting	Clotting	factor IX/Christmas factor/plasma thromboplastic component/hemophilia	306900	NM_000133	Xq27.1-q27.2
			factor X/Stuart factor	227600	NM_000504	13q34
Cardiovascular or (additional genes in Cardiovascular or and	Clotting	Clotting	factor XI/plasma thromboplastin antecedent	264900	NM_000128	4q35
			factor XII/Hageman factor	234000	NM_000505	5q33-qter
Cardiovascular or (additional genes in Cardiovascular or and	Clotting	Clotting	factor XIIIa1/fibrin-stabilizing factor	134570	NM_000129	6p25-p24
			prekallikrein/Fletcher factor	229000	*****	4q35
Cardiovascular or (additional genes in Cardiovascular or and	Clotting	Clotting	kininogen/Flaujeac factor	228960	*****	3q27
			solute carrier family 12, member 3/SLC12A3 (renal sodium/chloride transporter)	600968	NM_000339	16q13
Cardiovascular or (additional genes in Cardiovascular or and	Clotting	Clotting	renin/REN	179820	NM_000537	Xq28
			renin-binding protein/RENBP	312420	NM_002910	1q32
Cardiovascular or (additional genes in Cardiovascular or and	Clotting	Clotting	angiotensinogen/AGT	106150	NM_000029	1q42-q43
			angiotensin II type 1 receptor/AGTR1	106165	M87290	3q21-q25
Cardiovascular or (additional genes in Cardiovascular or and	Clotting	Clotting	guanine nucleotide binding protein (G protein), beta polypeptide 3/GNB3	139130	NM_002075	12p13

<i>Renal)</i>	Hemostasis		dipeptidyl carboxypeptidase I (angiotensin I converting enzyme)/ACE/DCP1	106180	NM_000789	17q23
		Natriuretic Peptide	atrial natriuretic peptide precursor A/NPPA	108780	X01471	1p36.2
			atrial natriuretic peptide precursor B/NPPB	600295	*****	1p36.2
			atrial natriuretic peptide precursor C/NPPC	600296	D28874	2q24-qter
			natriuretic peptide receptor A/ANPRA/NPR1	108960	*****	1q21-q22
			natriuretic peptide receptor B/ANPRB/NPR2	108961	*****	9p21-p12
			natriuretic peptide receptor C/ANPRC/NPR3	108962	NM_000908	5p14-p12
			endothelin 1/EDN1	131240	NM_001955	6p24-p23
			endothelin 2/EDN2	131241	NM_001956	1p34
			endothelin 3/EDN3	131242	NM_000114	20q13.2-q13.3
			endothelin converting enzyme 1/ECE1	600423	NM_001397	1p36.1
		Endothelin	endothelin A receptor isoform delta 3/EDNRA	131243	AF014826	Chr. 4
			endothelin receptor type B/EDNRB	131244	NM_000115	13q22
			cardiotrophin 1	600435	*****	*****
			leukemia inhibitory factor/LIF	159540	NM_002309	2q12.1-q12.2
			ciliary neurotrophic factor/CNTF	118945	NM_000614	11q12.2
			nerve growth factor alpha	162020	*****	*****
			nerve growth factor beta	162030	NM_005378	1p13.1
			nerve growth factor gamma			
			subunit/NGFG	162040	*****	19q13.3

**Growth
Factor**

neurotrophin 3/NTF3	162660	NM_002527	12p13
neurotrophin 5/NTF4/NTF5	162662	NM_006179	19q13.3
neurotrophin 6 alpha/NTF6A	604021	NM_004149	19q13.3
neurotrophin 6 beta/NTF6B	604022	NM_004150	chr. 19
neurotrophin 6 gamma/NTF6G	604023	NM_004151	chr. 19
brain derived neurotrophic	113505	*****	11p13
growth associated protein 43/GAP43	162060	NM_002045	Chr.3
pleiotrophin/NEGF1/PTN	162095	AH004121	7q33
semaphorin 3A/SEMA3A	603961	*****	*****
glial growth factor 2/neuregulin	142445	M94166	8p22-p11
neuregulin 2/NRG2	603818	*****	5q23-q33
neurite growth promoting factor			
2/NEGF2	162096	*****	11p11.2
glial cell derived neurotrophic			
factor/GDNF	600837	NM_000514	5p13.1-p12
insulin-like growth factor			
1/somatomedin C/IGF1	147440	M11568	12q22-q24.1
insulin-like growth factor			
2/somatomedin A/IGF2	147470	NM_000612	11p15.5
transforming growth factor/TGFB1	190180	M60315	9q13.1-q13.3
transforming growth factor/TGFB2	190220	M19154	1q41
transforming growth factor/TGFB3	190230	X14149	14q24
ciliary neurotrophic factor			
receptor/CNTFR	118946	NM_001842	9p13
nerve growth factor receptor/NGFR	162010	NM_002507	17q21-q22
neurotrophic tyrosine kinase receptor			
type 1/NTRK1	191315	Y09033	1q21-q22
neurotrophic tyrosine kinase receptor			
type 2/NTRK2	600456	NM_006180	9q22.1

**Growth
Factors and
Receptors**

neurotrophic tyrosine kinase receptor type 3/NTRK3	191316	NM_002530	15q25
reelin/RELN	600514	NM_005045	7q22
neuropilin 1/VEGF 165	602069	NM_003873	10p12
neuropilin 2/VEGF 165 receptor/NP2	602070	NM_003872	2q34
homolog of Drosophila	603448	AF071062	1p32-p31
retinoic acid receptor alpha/RARA	180240	NM_000964	17q12
retinoic acid receptor beta/RARB	180220	NM_000965	3p24
retinoic acid receptor gamma/RARG	180190	M57707	12q13
RAR related orphan receptor A/RORA	600825	NM_002943	15q21-q22
RAR related orphan receptor B/RORB	601972	*****	9q22
RAR related orphan receptor C/RORC	602943	NM_005060	1q21
retinoid X receptor alpha/RXRA	180245	NM_002957	9q34.3
retinoid X receptor beta/RXRB	180246	X66424	6p21.3
retinoid X receptor gamma/RXRG	180247	U38480	1q22-q23
vitamin B12 receptor/cubilin/CUBN	602997	NM_001081	10p12.1
vitamin D receptor/VDR	601769	NM_000376	12q12-q14
cannabinoid receptor 1/G protein- coupled/CNR1	114610	NM_001840	6q14-q15
oncogene ERBB3/HER3	190151	NM_001982	12q13
homolog 3 of Drosophila			
Notch/NOTCH3	600276	NM_000435	19p13.2-p13.1
SRC, FGR, YES-related oncogene			
FYN/FYN (receptor tyrosine kinase)	137025	NM_002037	6q21
receptor 1 for activated protein kinase C/RACK1	176981	*****	*****
insulin-like growth factor 1 receptor precursor/IGF1R	147370	NM_000875	15q25-q26
insulin-like growth factor 2 receptor/IGF2R	147280	NM_000876	6q26

Receptors

Growth and Differentiation on (additional genes in Oncology)	TGF-B type I receptor/TGFBRI	190181	AH006005	9q33-q34
	TGF-B type II receptor/TGFBRII	190182	NM_003242	3p22
	TGF-B type III receptor/TGFBRIII	600742	L07594	1p33-p32
	fibroblast growth factor receptor 1/FGFR1	136350	*****	8p11.2-p11.1
	fibroblast growth factor receptor 2/FGFR2	176943	Y17131	10q26
	fibroblast growth factor receptor 3/FGFR3	134934	NM_005247	4p16.3
	fibroblast growth factor receptor 4/FGFR4	134935	NM_002011	5q35.1-qter
	laforin/EPM2A	254780	AF084535	6q24
	steroid receptor coactivator 1/SRC1	602691	NM_003743	2p23
	glucocorticoid receptor interacting protein 1/GRIP1	601993	NM_006540	*****
	nuclear receptor coactivator/AIB1	601937	NM_006534	20q12
	p300/CBP associated factor/PCAF	602303	U57317	3p24
	CREB binding protein/CRB	600140	NM_004380	16p13.3
	cyclic AMP responsive element binding protein 1/CREB1	123810	NM_004379	2q32.3-q34
	silencing mediator for retinoid and thyroid hormone receptors/SMRT	600848	NM_006312	*****
	retinoic and thyroid hormone receptor associated corepressor 1/TRAC1/NCOR1	600849	NM_006311	*****
	steroid receptor RNA activator/SRA	603819	AF092038	chr. 5
	protein kinase, cAMP-dependent regulatory, type 1 beta/PRKAR1B	176911	*****	7pter-p22
	early growth response 2/EGR2	129010	NM_000399	0q21.1-q22.1

neuronal growth-associated protein SCG10/SCG10	600621	*****	*****
apoptosis-related cysteine protease 2/caspase 2/CASP2	600639	NM_006156	7q35
apoptosis-related cysteine protease 1/caspase 1/CASP1	147678	L27475	1q22.2-q22.3
neuronal apoptosis inhibitory protein/NAIP	600355	NM_004536	5q12.2-q13.3
protein kinase C, alpha/PRKCA	176960	NM_002737	17q22-q23.2
protein kinase C beta-II type/PRKCB1	176970	M13975	16p11.2
protein kinase C, delta/PRKCD	176977	NM_006254	3p
protein kinase C, epsilon/PRKCE	176975	NM_005400	2p21
protein kinase C, gamma/PRKCG	176980	*****	19q13.4
protein kinase C, iota/PRKCI	300094	NM_002740	Xq21.3
protein kinase C zeta/PRKCZ	176982	L14283	*****
protein kinase C-like 1/PRKCL1	601032	NM_002741	19p12
protein kinase C-like 2/PRKCL2	602549	NM_006256	*****
inositol polyphosphate-1- phosphatase/INPPI	147263	NM_002194	2q32
phosphodiesterase 1A, calmodulin- dependent/PDE1A	171890	NM_005019	Chr.4
phosphodiesterase 1B, calmodulin- dependent/PDE1B	171891	NM_000924	12q13
phosphodiesterase 1C, calmodulin- dependent/PDE1C	602987	NM_005020	*****
phosphodiesterase 4A, cAMP- specific/PDE4A	600126	NM_006202	19p13.2
phosphodiesterase 4B, cAMP- specific/PDE4B	600127	NM_002600	1p31

Signaling

Signaling

		phosphodiesterase 4C, cAMP-specific/PDE4C	600128	*****	Chr.19
		phosphodiesterase 4D, cAMP-specific/PDE4D	600129	NM_006203	5q12
		phosphodiesterase 7A, cAMP-specific/PDE7A	171885	L12052	8q13-q22
		phosphodiesterase 8A, cAMP-specific/PDE8A	602972	AF056490	*****
		phosphodiesterase 9A, cAMP-specific/PDE9A	602973	NM_002606	21q22.3
		telomerase protein component 1	601686	U86136	14q11.2
		telomerase reverse transcriptase	187270	AF015950	5p15.33
		telomerase RNA component	602322	U86046	3q21-q28
		superoxide dismutase 1/SOD1	147450	NM_000454	21q22.1
		superoxide dismutase 2, mitochondrial/SOD2	147460	X65965	6q25.3
		thioredoxin-dependent peroxide reductase/TDPXI	600538	NM_005809	13q12
		Peptide methionine sulfoxide reductase/MSRA	601250	*****	*****
		lipoprotein, Lp(a)/LPA	152200	NM_005577	6q27
		succinate dehydrogenase complex, subunit C, integral membrane protein/SDHC	602413	NM_003001	1q21
		glucose-6-phosphate dehydrogenase/G6PD (mitochondrial)	305900	NM_000402	Xq28
		aldehyde oxidase 1/AOX1	602841	NM_001159	2q33
		mitochondrial tRNA(lys)	590060	M37726	mitochondria
Oxygen Stress	Oxygen Stress				

Mitochondrial Maintenance	Translation	mitochondrial tRNA(ser)(UCN)	590080	S79597	mitochondria
		mitochondrial tRNA(Gln)	556500	S77916	mitochondria
		mitochondrial tRNA(Thr)	556500	S77921	mitochondria
	Protein Maturation	paraplegin (nuclear-encoded mitochondrial metalloprotease)	602783	NM_003119	16q24.3
Electron Transport		NADH-ubiquinone oxidoreductase flavoprotein 2, 24 kDa subunit/NDUFV2	600532	EG_D885428	p11.31-p11.3
		cytochrome oxidase subunit I/MTCO1	516030	AF035429	mitochondria
		cystatin B/stefin B/CSTB	601145	NM_000100	21q22.3
		cystatin C/CST3	105150	NM_000099	20p11.2
		ubiquitin carboxy-terminal esterase L1/UCHL1	191342	NM_004181	4p14
		ubiquitin-protein ligase E3A/UBE3A	601623	NM_000462	15q11-q13
		peptidyl-prolyl isomerase A/cyclophilin A/PPIA	123840	Y00052	7p13
		peptidyl-prolyl isomerase B/cyclophilin B/PPIB	123841	M60857	chr. 15
		peptidyl-prolyl isomerase C/cyclophilin C/PPIC	123842	S71018	*****
		peptidyl-prolyl isomerase D/cyclophilin D/PPID	601753	NM_005038	4q31.3
Protein Maturation and Catabolism		peptidyl-prolyl isomerase E/cyclophilin E/PPIE	*****	NM_006112	*****
		FK506 binding protein 1A/immunophilin/FKBP1A	186945	NM_000801	20p13
		FK506 binding protein 2/immunophilin/FKBP2	186946	NM_004470	1q13.1-q13.3

	FK506 binding protein 4/immunophilin/FKBP4	600611	NM_002014	*****
	FK506 binding protein 5/immunophilin/FKBP5	602623	*****	*****
	microsomal stress 70 protein ATPase core/STCH	601100	U04735	21q11.1
	heat shock protein, DNAJ-like 1/HSJ1	604139	X63368	2q32-q34
	heat shock protein, DNAJ-like 2/HSJ2	602837	NM_001539	*****
	alpha-B-crystallin/CRYAB	123590	M28638	1q22.3-q23.1
	heat shock transcription factor 1/HSF1	140580	NM_005526	*****
	heat shock transcription factor 2/HSF2	140581	NM_004506	*****
	heat shock transcription factor 4/HSF4	602438	NM_001538	16q21
	microtubule-associated protein tau/MAPT	157140	NM_005910	17q21.1
Cytoskeleton	tubulin, alpha, brain-specific/TUBA3	602529	NM_006009	2q
	beta-tubulin gene/TUBB	191130	J00314	6p21.3
	tubulin, beta, 5/TUBB5	602662	NM_006087	*****
	cadherin 2/NCAD/CDH2	114020	Z27440	18q11.2
	calpain, large polypeptide L3/CAPN3	114240	NM_000070	5q15.1-q21.1
	neural cell adhesion molecule	308840	X67912	Xq28
	neural cell adhesion molecule	116930	*****	11q23.1
	neural cell adhesion molecule	602040	NM_004540	21q21
	neural cell adhesion	601581	U55258	7q31.1-q31.2
Adhesion	opioid binding cell adhesion molecule/OBCAM	600632	*****	Chr.11
	nerve injury-induced protein 1/ninjurin/NINJ1	602062	NM_004148	9q22
	protease inhibitor 12	602445	NM_005025	*****

Biosynthesis	cathepsin B/b-aCTSBmyloid precursor protein secretase/CTSB	116810	M14221	8p22
	thimet oligopeptidase 1/THOP1	601117	NM_003249	19p13.3
	amyloid beta A4 precursor	104760	NM_000484	1q21.3-q22.0
	amyloid beta A4 precursor protein-like/APPL1	104740	*****	9q31-qter
Interacting Proteins	presenilin 1/PSEN1 (membrane/adhesion)	104311	NM_000021	14q24.3
	presenilin 2/PSEN2 (membrane/adhesion)	600759	NM_000447	1q31-q42
	amyloid beta A4 precursor protein-binding, family A, member 1/APBA1/MINT1	602414	NM_004664	9q13
	amyloid beta A4 precursor protein-binding, family A, member 1/APBA2	602712	*****	15q
	amyloid beta A4 precursor protein-binding, family B, member 1/APBB1	602709	NM_001164	11p15
	amyloid beta A4 precursor protein-binding, family B, member 1/APBB2	602710	U62325	Chr.4
	Munc 18-1 interacting protein	603452	*****	*****
	apolipoprotein E/APOE	107741	NM_000041	19q13.2
	c-jun	165160	J04111	1p32-p31
	low density lipoprotein receptor-related protein/LRP1	107770	NM_002332	2q13.1-q13.2
β-amyloid Metabolism	microtubule-associated protein tau/MAPT	157140	NM_005910	17q21.1
	synuclein alpha/SNCA	163890	NM_000345	4q21
	synuclein beta/SNCB	602569	NM_003085	5q35
	synuclein gamma/SNCG	602998	NM_003087	0q23.2-q23.3

Cellular Maintenance		hydroxyacyl-Coenzyme A dehydrogenase, type II/HADH2	602057	NM_004493	*****
		myeloperoxidase/MPO	254600	J02694	17q23.1
		mitogen activated protein kinase associated protein kinase 2/MAPKAPK2	602006	X75346	*****
Tau Phosphorylation State		protein phosphatase 2, structural/regulatory subunit A, beta/PPP2R1B	603113	*****	11q22-q24
		protein phosphatase 2, regulatory subunit B, alpha/PPP2R5A	601643	NM_006243	1q41
		protein phosphatase 2, regulatory subunit B, beta/PPP2R5B	601644	NM_006244	11q13
		protein phosphatase 2, regulatory subunit B, gamma/PPP2R5C	601645	NM_002719	3p21
		protein phosphatase 2, regulatory subunit B, delta/PPP2R1D	601646	NM_006245	6p21.1
		protein phosphatase 2, regulatory subunit B, epsilon/PPP2R1E	601647	NM_006246	7p12-p11.2
		Thimet oligopeptidase	601117	Z50115	19p13.3
		alpha-1-antichymotrypsin/AAC1	107280	NM_001085	14q32.1
		apoptosis-related cysteine protease 1/caspase 1/CASP3	600636	NM_004346	4q35
		alpha-2-macroglobulin/A2M	103950	NM_000014	2p13.3-p12.3
Catabolism		apolipoprotein A1 of HDL/APOA1	107680	NM_000039	11q23
		apolipoprotein A4/APOA4	107690	NM_000482	11q23
		apolipoprotein C1/APOC1	107710	NM_001645	19q13.2
		apolipoprotein D/APOD	107740	NM_001647	3q26.2-qter
		apolipoprotein E/APOE	107741	NM_000041	19q13.2
Transport					

Lipid Transport and Metabolism (additional genes below in Inflammation)	Uptake	apolipoprotein J/clustrin/APOJ/CLU	185430	NM_001831	8p21-p12
		low density lipoprotein receptor-related protein 1/LRP1	107770	NM_002332	2q13.1-q13.2
		low density lipoprotein receptor-related protein 2/LRP2	600073	U33837	2q24-q31
		low density lipoprotein receptor-related protein 5/LRP5	603506	AF077820	11q13.4
		low density lipoprotein receptor-related protein 8/LRP8	602600	NM_004631	1p34
		low density lipoprotein receptor-related protein-associated protein	104225	NM_002337	4p16.3
		oxidized low density lipoprotein receptor/OLR1	602601	NM_002543	12p13-p12
		very low density lipoprotein receptor/VLDLR	192977	S73732	9p24
		sortilin related receptor/SORL1	602005	U60975	1q23.2-q24.2
		plasma cholesterol ester transfer protein/CETP	118470	NM_000078	16q21
		phospholipid transfer protein/PLTP	172425	NM_006227	20q12-q13.1
		sterol-O-acyl transferase 1/SOAT1	102642	L21934	1q25
	Metabolism	sterol-O-acyl transferase 2/SOAT2	601311	*****	chr. 12
		HMGCoA reductase/HMGCR	142910	NM_000859	5q13.3-q14
		pyruvate dehydrogenase complex E1-alpha subunit/PDHA1	312170	L48690	Xp22.2-p22.1
		pyruvate dehydrogenase (lipoamide) beta subunit/PDHB	179060	NM_000925	3p13-q23
		pyruvate dehydrogenase complex E3 subunit/DLD	246900	NM_000108	7q31-q32
		sialyltransferase 8/GD3	601123	NM_003034	2p12.1-p11.2

Myelination	Myelination	hexosaminidase A (alpha polypeptide)/HEXA	272800	NM_000520	15q23-q24
		hexosaminidase B (beta)	268800	M34906	5q13
Myelination	Myelination	lysosomal acid beta-galactosidase	230500	S55851	3p21.33
		GM2 ganglioside activator protein/GM2A	272750	NM_000405	5q31.3-q33.1
Myelination	Myelination	UDP-Gal:betaGlcNAc beta 1,3-galactosyltransferase, polypeptide 2/B3GALT2	603095	NM_003783	6p21.3
		myelin proteolipid	312080	M27110	Xq22
Myelination	Myelination	Folate Receptor Alpha/FOLR1	136430	M28099	1q13.3-q13.5
		Folate Receptor Beta/FOLR2	136425	AF000380	1q13.3-q13.5
Myelination	Myelination	Folate Receptor Gamma/FOLR3	602469	Z32564	*****
		Folate Transporter (SLC19A1)	600424	U19720	21q22.3
Myelination	Myelination	Vitamin B12 binding protein	275350	NM_000355	22q11.2-qter
		folylpolyglutamate synthetase/FPGS	136510	M98045	9cen-q34
Myelination	Myelination	gamma-glutamyl hydrolase/GGH	601509	U55206	*****
		Methylenetetrahydrofolate reductase/MTHFR	236250	U09806	1p36.3
Myelination	Myelination	Dihydrofolate reductase/DHFR	126060	J00140	5q11.2-q13.2
		5,10-methylenetetrahydrofolate dehydrogenase, 5,10-methylenetetrahydrofolate cyclohydrolase, 10-formyltetrahydrofolate synthetase/MTHFD1	172460	NM_005956	14q24
Myelination	Myelination	5,10-methenyltetrahydrofolate synthetase (5-formyltetrahydrofolate cyclo-ligase)/MTHFS	604197	NM_006441	Chr. 15

Folate Metabolism	Metabolism				
	phosphoribosylglycinamide formyltransferase, phosphoribosylglycinamide synthetase,	138440	NM_000819	21q22.1	
	phosphate hydrolase 1/FOH1	600934	NP_004467	11q14	
	6-pyruvoyl tetrahydrobiopterin synthase/PTPS	261640	Q03393	1q22.3-q23.3	
	serine hydroxymethyltransferase 1 (soluble)/SHMT1	182144	NM_004169	17p11.2	
	serine hydroxymethyltransferase 2 (mitochondrial)/SHMT2	138450	NM_005412	12q13	
	Glycine aminotransferase/glycine cleavage T protein/GAT	238310	NM_000481	3p21.2-p21.1	
	5-methyltetrahydrofolate- homocysteine methyltransferase/methionine glutamate	156570	NM_000254	1q43	
	formiminotransferase/dihydrofolate synthetase	229100	*****	*****	
Carbon Unit Activation for SAM	methionine adenosyltransferase I, alpha/MAT1A	250850	NM_000429	10q22	
	methionine adenosyltransferase II, alpha/MAT2A	601468	NM_005911	2p11.2	

Table 3. ADME and Toxicology Gene List

Class	Pathway	Function	Name	OMIM	GID	Locus
			sucrase-isomaltase/SI	222900	NM_001041	3q25-q26

Glycosidases	maltase-glucoamylase/alpha-glucosidase/MGAM	154360	NM_004668	Chr.7
	lactase-phlorizin hydrolase/LPH/lactase/LCT	603202	NM_002299	2q21
	salivary amylase A/AMY1A	104700	NM_004038	1p21
	salivary amylase B/AMY1B	104701	*****	1p21
	salivary amylase C/AMY1C	104702	*****	1p22
	pancreatic amylase A/AMY2A	104650	X07057	1p21
	pancreatic amylase B/AMY2B	104660	*****	1p21
	dipeptidylpeptidase IV/CD26/ADA complexing protein 2/DPP4	102720	NM_001935	2q23
	pepsinogen A/PGA/PG	169700	AH001519	11q13
	pepsinogen, group 3/PGA3	169710	*****	11q13
	pepsinogen C/PGC	169740	J04443	6p21.3-p21.1
	kallikrein 1/KLK1	147910	AH002853	19q13.2-q13.4
	chymotrypsin-like protease	118888	X71875	16q22.1
	trypsinogen 1/TRY1/protease, serine 1/PRSS1	276000	NM_002769	7q35
	trypsinogen 1/TRY2/protease, serine 2/PRSS2	601564	NM_002770	7q35
	trypsinogen 1/TRY3/protease, serine 3/PRSS3	*****	NM_002771	*****
	enterokinase 1/TRY3/protease, serine 7/PRSS7	226200	NM_002772	21q21

Dactatene

Gastrointestinal Drug Metabolism	Proteases and Peptidases	chymotrypsinogen 1/CTRB1	118890	NM_001906	16q23.2-q23.3
		carboxypeptidase A1/CPA1	114850	NM_001868	7q32-qter
		carboxypeptidase A2/CPA2	600688	NM_001869	*****
		carboxypeptidase Z/CPZ	603105	NM_003652	
		elastase 1/ELA1	130120	D00158	12q13
		renal microsomal dipeptidase/DPEP1 (b-lactam ring hydrolysis)	179780	NM_004413	16q24.3
		tripeptidyl peptidase II/TPP2	190470	NM_003291	13q32-q33
		protease inhibitor 1/alpha-1-antitrypsin/AAT/PI	107400	NM_000295	14q32.1
		protease inhibitor/alpha-1-antichymotrypsin/AAC1	107280	NM_001085	14q32.1
		protease inhibitor 1 (alpha-1-antitrypsin)-like/PIL	107410	NM_006220	14q32.1
	Lipases	Carboxyl ester lipase (bile salt-stimulated lipase)/CEL	114840	M85201	9q34.3
		Carboxyl ester lipase-like (bile salt-stimulated lipase-like)/CELL	114841	NM_001808	9q34.3
		Pancreatic colipase/CLPS	120105	M95529	6pter-p21.1
		Pancreatic triglyceride lipase/PNLIP	246600	AH003527	10q26.1
		Lipoprotein lipase/LPL	238600	NM_000237	8p22
		Hepatic triglyceride lipase/LIPC	151670	AH005429	

Oxidases	salivary peroxidase/SAPX	170990	U39573	*****
	alcohol dehydrogenases 6/ADH6	103735	NM_000672	15q26
Esterases	paraoxonase 2/PON2	602447	L48513	7q21.3
Phosphatases	intestinal alkaline phosphatase/ALPI	171740	NM_001631	2q36.3-q37.1
	tissue non-specific alkaline phosphatase/liver alkaline phosphatase/ALPL	171760	NM_000478	1p36.1-p34
	serum albumin/ALB	103600	NM_000477	4q11-q13
Blood Transport	alpha fetoprotein/AFP	104150	NM_001134	4q11-q13
	alpha albumin/afamin/AFM/ALB2	104145	NM_001133	4q11-q13
	vitamin D-binding protein/group-specific component/GC	139200	AH004448	4q12
	orosomucoid 1/alpha 1 acid glycoprotein/ORM1	138600	M13692	9q34.1-q34.3
	orosomucoid 2/alpha 1 acid glycoprotein, type 2/ORM2	138610	NM_000608	9q34.1-q34.3
	transthyretin (prealbumin, amyloidosis type I)/TTR	176300	NM_000371	18q11.2-q12.1
	thyroxin-binding globulin/TBG	314200	NM_000354	Xq22.2
	corticosteroid binding globulin precursor/CBG	122500	NM_001756	14q32.1
	sex hormone-binding globulin/SHBG	182205	X16349	17p13-p12
Drug Binding				

	mannose-binding lectin, soluble/MBL2	154545	NM_00024 2	10q11.2- q21
Bile Acid Binders	Hepatic fatty acid binding protein/FABP1	134650	*****	2p11
	Intestinal fatty acid binding protein/FABP2	134640	NM_00013 4	4q28-q31
	Muscle fatty acid binding protein/mammary-derived growth inhibitor/MDGI/FABP3	134651	NM_00410 2	1p33-p31
	Adipocyte fatty acid binding protein/FABP4	600434	NM_00144 2	8q21
	Ileal fatty acid binding protein/FABP6	600422	U19869	5q23-q35
	Brain fatty acid binding protein/FABP7	602965	D88648	6q22-q23
	Adipocyte long chain fatty acid transport protein/FATP	600691	*****	*****
	Retina-specific ATP binding cassette transporter/ABCR	601691	NM_00035 0	1p21-p13
	ATP binding cassette 1/ABC1	600046	AJ012376	9q22-q31
	ATP binding cassette 2/ABC2	600047	U18235	9q34
	ATP binding cassette 3/ABC3	601615	NM_00108 9	16p13.3
	ATP binding cassette 7/ABC7	300135	AB005289	Xq13.1- q13.3
	ATP binding cassette 8/ABC8	603076	AF038175	21q22.3
	ATP-binding cassette 50/ABC50	603429	AF027302	6p21.33
	Placenta-specific ATP-binding cassette transporter/ABCP	603756	NM_00482 7	4q22

cystic fibrosis transmembrane conductance regulator/CFTR	602421	NM_000492	7q31.2
adrenoleukodystrophy/adrenomyeloneuropathy/ALD	300100	NM_000033	Xq28
adrenoleukodystrophy related protein/ALDR	601081	U28150	12q11-q12
sulfonylurea receptor (hyperinsulinemia)/SUR	600509	NM_000352	11p15.1
peroxisomal membrane protein 1/PXMP1	170995	NM_002858	1p22-p21
peroxisomal membrane protein 1-like/PXMP1L	603214	NM_005500	14q24.3
antigen peptide transporter 1/MHC 1/TAP1	170260	NM_000593	6p21.3
antigen peptide transporter 2/MHC 2/TAP2	170261	NM_000544	6p21.3
multidrug resistance associated protein MRP1	158343	L05628	16p13.1
multidrug resistance associated protein MRP2/CMOAT	601107	NM_000392	10q24
ATP-binding cassette, sub-family C (CFTR/MRP), member 3/CMOAT2	*****	NM_003786	*****
ATP-binding cassette, sub-family C (CFTR/MRP), member 4/MOATB	*****	NM_005845	*****
ATP-binding cassette, sub-family C (CFTR/MRP), member 5/SMRP	*****	NM_005688	*****
ATP-binding cassette, sub-family C (CFTR/MRP), member 9/SUR2	601439	NM_005691	*****

ABC Transporters

**Absorption
and
Distribution**

multidrug resistance protein MDR1	171050	X96395	7q21.1
multidrug resistance protein MDR3/P-glycoprotein 3/PGY3	602347	X06181	7q21.1
anthracycline resistance-related protein/ARA	603234	NM_001171	16p13.1
bile salt export pump/BSEP	603201	NM_003742	2q24
familial intrahepatic cholestasis 1/FIC1	602397	NM_005603	18q21
Human sorcin/SRI	182520	L12387	7q21.1
Solute carrier family 1, member 1/SLC1A1 (glutamate)	133550	U08989	9p24
Solute carrier family 1, member 2/SLC1A2 (glutamate)	600300	U03505	11p13-p12
Solute carrier family 1, member 3/SLC1A3 (glutamate)	600111	U03504	5p13
Solute carrier family 1, member 4/SLC1A4 (glutamate)	600229	NM_003038	2p15-p13
Solute carrier family 1, member 5/SLC1A5 (neutral AA)	109190	AF105230	19q13.3
Solute carrier family 1, member 6/SLC1A6 (glutamate)	600637	NM_005071	*****
Solute carrier family 2, member 1/SLC2A1/SGLT1 (glucose)	182380	NM_006516	22q13.1
Solute carrier family 2, member 2/SLC2A2/GLUT2 (glucose)	138160	NM_006516	3q26.1-q26.3
Solute carrier family 2, member 3/SLC2A3/GLUT3 (glucose)	138170	M20681	12p13.3

Solute carrier family 2, member 4/SLC2A4/GLUT4 (glucose)	138190	*****	17p13
Solute carrier family 2, member 5/SLC2A5/GLUT5 (glucose)	138230	NM_003039	1p36.2
Solute carrier family 3 member 1/SLC3A1 (aa transporter)	104614	*****	2p16.3
Solute carrier family 5 member 1/SLC5A2 (glucose)	182381	*****	16p11.2
Solute carrier family 5 member 3/SLC5A3 (myoinositol)	600444	L38500	21q22
Solute carrier family 5 member 6/SLC5A6 (folate, biotin, lipoate)	604024	*****	2p23
Solute carrier family 6 member 1/SLC6A1 (GABA)	137165	X54673	3p25-p24
Solute carrier family 6 member 2/SLC6A2 (noradrenalin)	163970	NM_001043	16q12.2
Solute carrier family 6 member 3/SLC6A3 (dopamine)	126455	L24178	5p15.3
Solute carrier family 6 member 4/SLC6A4 (serotonin)	182138	X70697	17q11.1-q12
Solute carrier family 6, member 5/SLC6A5 (glycine)	604159	NM_004211	*****
Solute carrier family 6, member 6/SLC6A6 (taurine)	186854	U16120	3p25-q24
Solute carrier family 6, member 8/SLC6A8 (creatine)	300036	NM_005629	300036
Solute carrier family 6, member 9/SLC6A9 (glycine)	601019	S70612	1p33

Drug Uptake

Solute carrier family 6, member 10/SLC6A10 (creatine-testis)	601294	*****	16p11.2
Solute carrier family 6, member 12/SLC6A12 (GABA-betaine)	603080	NM_003044	12p13
Solute carrier family 7, member 1/SLC7A1 (cationic AA)	104615	*****	13q12.3
Solute carrier family 7, member 2/SLC7A2 (cationic AA)	601872	D29990	8p22
Solute carrier family 7, member 4/SLC7A4 (cationic AA)	603752	*****	22q11.2
Solute carrier family 7, member 5/SLC7A5 (neutral AA)	600182	M80244	16q24.3
Solute carrier family 7, member 7/SLC7A7 (dibasic AA)	603593	Y18474	14q11.2
Solute carrier family 7, member 9/SLC7A9 (neutral AA)	604144	*****	19q13.1
Solute carrier family 10, member 1/SLC10A1 (taurocholate)	182396	NM_003049	chr. 14
Solute carrier family 10, member 2/SLC10A2 (taurocholate)	601295	NM_000452	13q33
Solute carrier family 11, member 1/SLC11A1 (?)	600266	AH002806	2q35
Solute carrier family 11, member 2/SLC11A2 (iron)	600523	L37347	12q13
Solute carrier family 13, member 2/SLC13A2 (dicarboxylic acids)	604148	NM_003984	17p11.1-q11.1
Solute carrier family 14, member 1/SLC14A1 (urea)	111000	*****	18q11-q12

**Solute
Antiporters**

Solute carrier family 14, member 2/SLC14A2 (urea)	601611	X96969	18q12.1-q21.1
Solute carrier family 15, member 1/SLC15A1 (peptides)	600544	U13173	13q33-q34
Solute carrier family 15, member 2/SLC15A2 (peptides)	602339	S78203	*****
Solute carrier family 16, member 1/SLC16A1 (monocarboxylic acids)	600682	NM_003051	1p13.2-p12
Solute carrier family 16, member 2/SLC16A2 (monocarboxylic acids)	300095	NM_006517	Xq13.2
Solute carrier family 16, member 3/SLC16A3 (monocarboxylic acids)	603877	NM_004207	*****
Solute carrier family 16, member 4/SLC16A4 (monocarboxylic acids)	603878	*****	*****
Solute carrier family 16, member 5/SLC16A5 (monocarboxylic acids)	603879	NM_004695	*****
Solute carrier family 16, member 6/SLC16A6 (monocarboxylic acids)	603880	NM_004694	*****
Solute carrier family 16, member 7/SLC16A7 (monocarboxylic acids)	603654	AF049608	12q13
Solute carrier family 18, member 1/VAT1/SLC18A1 (monoamines)	193001	L09118	10q25
Solute carrier family 18, member 2/VAT2/SLC18A2 (monoamines)	193002	*****	8p21.3
Solute carrier family 18, member 3/VAT3/SLC18A3 (monoamines)	600336	NM_003055	10q11.2
Solute carrier family 19, member 1/SLC19A1 (reduced folate)	600424	U19720	21q22.3

Solute carrier family 19, member 2/SLC19A2 (thiamine)	603941	AF160186	1q23.2-q23.3
Solute carrier family 21, member 2/SLC21A2 (prostaglandin)	601460	NM_005630	3q21
Solute carrier family 21, member 3/SLC21A3 (organic anion)	602883	NM_005075	12p12
Solute carrier family 22, member 1/SLC22A1 (organic cation)	602607	NM_003058	6q26
Solute carrier family 22, member 1-like/SLC22A1L (organic cation)	602631	AF037064	11p15.5
Solute carrier family 22, member 2/SLC22A2 (organic cation)	602608	NM_003058	6q26
Solute carrier family 22, member 4/SLC22A4 (organic cation)	604190	NM_003059	Chr. 5
Solute carrier family 22, member 5/SLC22A5 (carnitine)	603377	NM_003060	5q33.1
Solute carrier family 25, member 1/SLC25A1 (tricarboxylic acids) (mitochondrial)	190315	X96924	22q11
Solute carrier family 25, member 11/SLC25A11 (oxoglutarate/malate) (mitochondrial)	604165	NM_003562	17p13.3
Solute carrier family 25, member 12/SLC25A12 (?) (mitochondrial)	603667	NM_003705	*****
Solute carrier family 25, member 13/SLC25A13 (?) (mitochondrial)	603859	*****	7q21.3

Solute carrier family 25, member 15/SLC25A15 (ornithine) (mitochondrial)	603861	*****	13q14
Solute carrier family 25, member 16/SLC25A16 (ADP/ATP) (mitochondrial)	139080	M31659	10q21.3-q22.1
Solute carrier family 29, member 1/SLC29A1/ENT1 (nucleoside) (mitochondrial)	602193	NM_004955	6p21.2-p21.1
Solute carrier family 29, member 2/SLC29A2/ENT2 (nucleoside) (mitochondrial)	602110	X86681	11q13
Aryl hydrocarbon receptor nuclear translocator/ARNT	126110	NM_001668	1q21
Aryl hydrocarbon receptor nuclear translocator-like/ARNTL	602550	NM_001178	11p15
Aryl hydrocarbon receptor/AHR	600253	NM_001621	7p15
Nuclear receptor subfamily 1, group I, member 2/NR1I2	603065	NM_003889	*****
Constitutive androstane receptor, beta/orphan nuclear hormone receptor/CAR	603881	NM_005122	*****
Nuclear receptor subfamily 1, group H, member 2/NR1H2	600380	U07132	19q13.3
Retinoic acid receptor, alpha/RARA	180240	NM_000964	17q12
Retinoic acid receptor, beta/RARB	180220	NM_000965	3p24

Retinoic acid receptor, gamma/RARG	180190	M57707	12q13
Retinoid X receptor alpha/RXRA	180245	NM_005693	9q34.3
Retinoid X receptor beta/RXRB	180246	X66424	6p21.3
Retinoid X receptor gamma/RXRG	180247	U38480	1q22-q23
RAR-related orphan receptor A/RORA	600825	NM_002943	15q21-q22
RAR-related orphan receptor B/RORB	600825	*****	15q21-q22
RAR-related orphan receptor C/RORC	602943	NM_005060	1q21
cellular retinoic acid-binding protein, type 2/CRABP2	180231	*****	1q21.3
glucocorticoid receptor/GRL	138040	NM_000176	5q31
Peroxisome proliferative activated receptor, alpha/PPARA	170998	NM_005036	22q12-q13.1
Peroxisome proliferative activated receptor, gamma/PPARG	601487	NM_005037	3p25
Peroxisome proliferative activated receptor, delta/PPARD	6E+05	NM_006238	1q21.3
cytochrome P450, subfamily I, polypeptide 1 (aryl hydrocarbon oxidase)/CYP1A1	108330	NM_000499	15q22-q24
cytochrome P450, subfamily I, polypeptide 2 (phenacetin metabolism)/CYP1A2	124060	AH002667	15q22-qter
cytochrome P450, subfamily IB, polypeptide 1 (dioxin inducible)/CYP1B1	601771	NM_000104	2p22-p21

cytochrome P450, subfamily II, polypeptide 1 (phenobarbital inducible)/CYP2A	123960	X13897	19q13.2
cytochrome P450, subfamily IIA, polypeptide 6 (coumarin-7- hydroxylase)/CYP2A6	122720	NM_00076 2	19q13.2
cytochrome P450, subfamily IIB (phenobarbital inducible)/CYP2B	123930	M29874	19q13.2
cytochrome P450, subfamily IIC, polypeptide 8/CYP2C8	601129	*****	10q24
cytochrome P450, subfamily IIC, polypeptide 9 (hydroxylation of tolbutamide)/CYP2C9	601130	*****	10q24
cytochrome P450, subfamily IIC, polypeptide 18/CYP2C18	601131	*****	10q25
cytochrome P450, subfamily IIC, polypeptide 19 (mephenytoin 4- hydroxylase)/CYP2C19	124020	NM_00076 9	10q24.1- q24.3
cytochrome P450, subfamily IID, polypeptide 6 (debrisoquine hydroxylation)/CYP2D6	124030	NM_00010 6	22q13.1
cytochrome P450, subfamily IIE (ethanol inducible)/CYP2E	124040	J02843	10q24.3- qter
cytochrome P450, subfamily IIF (ethoxycoumarin monooxygenase), polypeptide 1/CYP2F1	124070	NM_00077 4	19q13.2
cytochrome P450, subfamily IJ (arachidonate epoxidase), polypeptide 2/CYP2J2	601258	NM_00077 5	1p31.3- p31.2

**P450
Cytochromes
and
Regulatory
Factors**

**Cytochrome
P450s**

cytochrome P450, subfamily IIIA (niphedipine oxidase), polypeptide 3/CYP3A4	124010	NM_00077 6	7q22.1
cytochrome P450, subfamily IVA (fatty acid W-hydroxylase), polypeptide 11/CYP4A11	601310	NM_00077 8	Chr.1
cytochrome P450, subfamily IVB, polypeptide 1/CYP4B1	124075	NM_00077 9	1p34-p12
cytochrome P450, subfamily IVF (leukotriene B4-W-hydroxylase), polypeptide 3/CYP4F3	601270	NM_00089 6	19p13.2
cytochrome P450, subfamily VIIA (cholesterol 7-a-hydroxylase), polypeptide 1/CYP7A1	118455	M89803	8q11-q12
cytochrome P450, subfamily VIIB (oxysterol 7-a-hydroxylase), polypeptide 1/CYP7B1	603711	AF029403	8q21.3
cytochrome P450, subfamily VIIB (sterol 12-a-hydroxylase), polypeptide 1/CYP8B1	602172	*****	3p21.3-p22
cytochrome P450, subfamily XIA (cholesterol side-chain cleavage)/CYP11A	118485	NM_00078 1	15q23-q24
cytochrome P450, subfamily XIB, polypeptide 2 (steroid 11-b- hydroxylase)/CYP11B2	124080	NM_00049 8	8q21
cytochrome P450, subfamily XIX (androgen aromatase)/CYP19	107910	NM_00010 3	15q21.1
cytochrome P450, subfamily XXI (sterol 21-a-hydroxylase)/CYP21	201910	M13936	6p21.3

Phase I Drug Metabolism (oxidation and		cytochrome P450, subfamily XXIV (25-hydroxyvitamin D 24-hydroxylase)/CYP24	600125	S67623	20q13.2-q13.3
		cytochrome P450, subfamily XXVIA, polypeptide 1 (retinoic acid hydroxylase)/CYP26A1	602239	NM_000783	10q23-q24
		cytochrome P450, subfamily XXVIA, polypeptide 1 (25-hydroxyvitamin D-1- α -hydroxylase)/CYP27A1	213700	NM_000105	2q33-qter
		adrenodoxin/ferredoxin 1/FDX1/ADX	103260	NM_004109	11q22
		adrenodoxin reductase/ferredoxin:NADP(+) reductase/FDXR/ADX	103270	NM_004110	17q24-q25
		cytochrome P450, subfamily XXVIB, polypeptide 1 (25-hydroxyvitamin D-1- α -hydroxylase)/CYP27B1	264700	NM_000785	12q14
		cytochrome P450, subfamily XLVI (cholesterol 24-hydroxylase)/CYP46	604087	NM_006668	14q32.1
		cytochrome P450, subfamily LI (lanosterol 14- α -demethylase)/CYP51	601637	U51692	7q21.2-q21.3
	Cofactor Synthesis	heme	603707	AJ224328	6p21.3
		heme	603708	*****	5q11
	Alcohol	alcohol dehydrogenases 1, alpha subunit/ADH1	103700	NM_000667	4q22
		alcohol dehydrogenases 2, beta subunit/ADH2	103720	NM_000668	4q22
		alcohol dehydrogenases 3, gamma subunit/ADH3	103730	M12272	4q22

reduction)	Dehydrogenases	alcohol dehydrogenases 4/pi isozyme/ADH4	103740	M15943	4q22
		alcohol dehydrogenases 5/chi isozyme/ADH5	103710	NM_000671	4q21-q25
		alcohol dehydrogenases 6/ADH6	103735	NM_000672	15q26
		alcohol dehydrogenases 7/ADH7	600086	AH006682	4q23-q24
Aldehyde Dehydrogenases	Aldehyde Dehydrogenases	aldehyde dehydrogenase 1/ALDH1 (liver cytosol)	100640	AH002598	9q21
		aldehyde dehydrogenase 2/ALDH2 (liver mitochondria)	100650	K03001	12q24.2
		aldehyde dehydrogenase 3/acetalddehyde	100660	M74542	17p11.2
		aldehyde dehydrogenase 4/ALDH4 (liver)	100670	NM_000692	9p13
		aldehyde dehydrogenase 5, member A1/succinic semialdehyde dehydrogenase/ALDH5A1	271980	NM_001080	6p22
		aldehyde dehydrogenase 6/acetalddehyde	600463	NM_000693	15q26
		aldehyde dehydrogenase 7/acetalddehyde	600466	NM_000694	11q13
		aldehyde dehydrogenase 8/ALDH8	601917	NM_000695	chr. 11
		aldehyde dehydrogenase 9/g-aminobutyraldehyde dehydrogenase/ALDH9	602733	NM_000696	1q22-q23
		aldehyde dehydrogenase 10/ALDH10	270200	NM_000382	17p11.2
Pyridine Nucleotide-Linked Oxidoreductases	Pyridine Nucleotide-Linked Oxidoreductases				

Aldo-Keto Reductases	Aldo-keto reductase family 1, member A1/dihydrodiol dehydrogenase/AKR1A1	103830	NM_00606 6	1p33-p32
	Aldo-keto reductase family 1, member C1/dihydrodiol dehydrogenase/AKR1C1	600449	NM_00135 3	10p15-p14
	Aldo-keto reductase family 1, member C3/dihydrodiol dehydrogenase/AKR1C3	603966	NM_00373 9	10p15-p14
	Aldo-keto reductase family 1, member C4/chlorodecone reductase/AKR1C4	600451	*****	10p15-p14
	Aldo-keto reductase family 7, member A2/aflatoxin aldehyde reductase/AKR7A2	603418	NM_00368 9	*****
	Carbonyl reductase 1/CBR1	114830	NM_00175 7	21q22.12
	Carbonyl reductase 2/CBR2	*****	*****	chr. 11
	Carbonyl reductase 3/CBR3	603608	NM_00123 6	21q22.2
	Sepiapterin reductase (7,8- dihydrobiopterin:NADP+ oxidoreductase)/SPR	182125	NM_00312 4	2p14-p12
	Z-crystallin/quinone reductase/CRYZ	123691	L31521	1p31-p22
Quinone Oxidoreductases	Z-crystallin-like/quinone reductase- like/CRYZL1	603920	NM_00511 1	21q22.1
	NAD(P)H menadione oxidoreductase 1, dioxin- inducible/NMOR1/diaphorase 4/DIA4	125860	NM_00090 3	16q22.1

		NAD(P)H menadione oxidoreductase 2, dioxin-inducible/NMOR2	160998	NM_00090 4	6pter-q12
		Flavin-containing monooxygenase 1/FMO1	136130	NM_00202 1	1q23-q25
		Flavin-containing monooxygenase 3/FMO3	136132	AH006707	1q23-q25
		Flavin-containing monooxygenase 4/FMO4	136131	NM_00146 0	1q23-q25
		Flavin-containing monooxygenase 5/FMO5	603957	NM_00146 1	1q21.1
	Flavin- Dependent Oxidoreductases	Monoamine Oxidase A; MAOA	309850	M69226	Xp11.23
		Monoamine Oxidase B; MAOB	309860	M69177	Xp11.23
		Xanthine dehydrogenase/XDH	278300	NM_00037 9	2p23-p22
		Aldehyde oxidase 1/AOX1	602841	NM_00115 9	2q33
		Copper-containing amine oxidase/AOC3	603735	NM_00373 4	17q21
		sulfite oxidase/SUOX	272300	NM_00045 6	*****
		Dihydropyrimidine dehydrogenase (5- fluorouracil detoxification)	274270	U09178	1p22
	Peroxisome Proliferation	Peroxisome proliferative activated receptor, alpha/PPARA	170998	NM_00503 6	22q12- q13.1
		Peroxisome proliferative activated receptor, gamma/PPARG	601487	NM_00503 7	3p25
		Peroxisome proliferative activated receptor, delta/PPARD	180231	NM_00623 8	1q21.3
		peroxisome biogenesis factor 1/PEX1	602136	AB008112	7q21-q22

Peroxisome Synthesis	peroxisomal membrane protein 3 (35kD)	170993	NM_000318	8q21.1
	peroxisomal biogenesis factor 3/PEX3	603164	NM_003630	*****
	peroxisomal biogenesis factor 6/PEX6	601498	NM_000287	6p21.1
	peroxisomal biogenesis factor 7/PEX7	601757	NM_000288	6q22-q24
	peroxisomal biogenesis factor 10/PEX10	602859	*****	*****
	peroxisomal biogenesis factor 11A/PEX11A	603866	NM_003847	*****
	peroxisomal biogenesis factor 11B/PEX11B	603867	NM_003846	*****
	peroxisomal biogenesis factor 12/PEX12	601758	NM_000286	
	peroxisomal biogenesis factor 13/PEX13	601789	U71374	2p15
	peroxisomal biogenesis factor 14/PEX14	601791	*****	*****
Fatty Acid β- Oxidation	peroxisomal farnesylated protein/PXFP	600279	NM_002857	1q22
	Fatty acid CoA Ligase, long chain 1/FACL1	152425	*****	3q13
	Fatty acid CoA Ligase, long chain 2/FACL2	152426	*****	4q34-q35
	Fatty acid CoA Ligase, long chain 3/FACL3	602371	NM_00445 7	2q34-q35
	Fatty acid CoA Ligase, long chain 4/FACL4	300157	NM_00445 8	Xq22.3
	Fatty acid CoA Ligase, very long chain 1/FACVL1	603247	*****	15q21.2
	Enoyl-CoA, hydratase/3-hydroxyacyl CoA dehydrogenase/EHHADH	261515	NM_00196 6	3q27
	hydroxyacyl-CoA dehydrogenase/3- ketoacyl-CoA thiolase/enoyl-CoA hydratase, alpha subunit/HADHA	600890	NM_00018 2	2p23
	hydroxyacyl-CoA dehydrogenase/3- ketoacyl-CoA thiolase/enoyl-CoA hydratase, beta subunit/HADHB	143450	NM_00018 3	2p23

Oxidation	acyl-Coenzyme A oxidase 1/ACOX1 (peroxisomal)	264470	NM_004035	17q25
	acyl-Coenzyme A oxidase 2, branched chain/ACOX2 (peroxisomal)	601641	NM_003500	3p14.3
	acyl-Coenzyme A dehydrogenase, C-2 to C-3 short chain precursor/ACADS (mitochondrial)	201470	NM_000017	12q22-qter
	acyl-Coenzyme A dehydrogenase, C-4 to C-12 straight chain/ACADM (mitochondrial)	201450	NM_000016	1p31
	acyl-Coenzyme A dehydrogenase, long chain/ACADL (mitochondrial)	201460	NM_001608	2q34-q35
	hydroxyacyl-Coenzyme A dehydrogenase, type II/HADH2	602057	NM_004493	*****
	enoyl-Coenzyme A hydratase 1/ECH1 (peroxisomal)	600696	NM_001398	19q13
	3-prime-phosphoadenosine 5-prime-phosphosulfate synthase 1/PAPSS1	603262	NM_005443	4q
	Phenol-preferring sulfotransferase, family 1A, member 1/SULT1A1	171150	NM_001055	16p12.1-p11.2
	Phenol-preferring sulfotransferase, family 1A, member 2/SULT1A2	601292	NM_001054	16p12.1-p11.2
Sulfate Unit Activation	Phenol-preferring sulfotransferase, family 1A, member 3/SULT1A3	600641	L19956	16p11.2
	Sulfotransferase, family 1C, member 3/SULT1C1	602385	U66036	2q11.1-q11.2
	Dehydroepiandrosterone (DHEA)-preferring sulfotransferase, family 2A, member 1/SULT2A1	125263	NM_003167	19q13.3

Sulfation	Sulfotransferase, family 2B, member 1/SULT2B1	604125	NM_004605	19q13.3
	Estrogen-preferring sulfotransferase/STE	600043	NM_005420	4q13.1
	N-deacetylase/N-sulfotransferase (heparan glucosaminyl)/NDST1	600853	U18918	5q32-q33.3
	N-deacetylase/N-sulfotransferase (heparan glucosaminyl)/NDST2	603268	NM_003635	10q22
	N-deacetylase/N-sulfotransferase (heparan glucosaminyl)/NDST3	603950	NM_004784	*****
	Carbohydrate sulfotransferase 1 (chondroitin 6/keratan)/CHST1	603797	NM_003654	11p11.2-p11.1
	Carbohydrate sulfotransferase 2 (chondroitin 6/keratan)/CHST2	603798	*****	7q31
	Carbohydrate sulfotransferase 3 (chondroitin 6/keratan)/CHST3	603799	NM_004273	*****
	Cerebroside sulfotransferase (3'-phosphoadenylylsulfate:galactosylceramide 3'')/CST	602300	NM_004861	*****
	Heparan sulfate (glucosamine) 3-O-sulfotransferase 1/HS3ST1	603244	NM_005114	*****
	Heparan sulfate (glucosamine) 3-O-sulfotransferase 2/HS3ST2	604056	NM_006043	16p12
	Heparan sulfate (glucosamine) 3-O-sulfotransferase 3A1/HS3ST3A1	604057	NM_006042	17p12-p11.2
	Heparan sulfate (glucosamine) 3-O-sulfotransferase 3B1/HS3ST3B1	604058	NM_006041	17p12-p11.2
	Heparan sulfate (glucosamine) 3-O-sulfotransferase 4/HS3ST4	604059	AF105378	16p11.2

Sulphydrylation	Methylguanine methyltransferase (O6-alkylguanine detoxification)	156569	M29971	10q26
	thiotransferase/rhodanese/TST (amide detoxification)	180370	D87292	22q11.2-qter
UDP-Glycosyltransferases	UDP glycosyltransferase 1/UGT1	191740	NM_001072	Chr. 12
	UDP glycosyltransferase family 2, member B4/UGT2B4	600067	NM_001073	4q13
	UDP glycosyltransferase family 2, member B7/UGT2B7	600068	NM_001074	1q14
	UDP glycosyltransferase family 2, member B10/UGT2B10	600070	NM_001075	*****
	UDP glycosyltransferase family 2, member B15/UGT2B15	600069	U06641	4q13
	UDP glycosyltransferase family 2, member B17/UGT2B17	601903	NM_001077	1q14
	UDP glycosyltransferase 8/UGT8	601291	U30930	4q26
	UDP-glucuronosyltransferase	218800	AJ005162	Chr. 2
	methionine adenosyltransferase I, alpha/MAT1A	250850	NM_000429	10q22
	methionine adenosyltransferase II, alpha/MAT2A	601468	NM_005911	2p11.2
Carbon Unit Activation for SAM	Folate Receptor Alpha/FOLR1	136430	M28099	1q13.3-q13.5
	Folate Receptor Beta/FOLR2	136425	AF000380	1q13.3-q13.5
	Folate Receptor Gamma/FOLR3	602469	Z32564	*****
	Folate Transporter (SLC19A1)	600424	U19720	21q22.3
	Vitamin B12 binding protein	275350	NM_000355	22q11.2-qter
	folypolyglutamate synthetase/FPGS	136510	M98045	9cen-q34
	gamma-glutamyl hydrolase/GGH	601509	U55206	*****

Conjugation	Carbon Unit Activation for Folate	Methylenetetrahydrofolate reductase/MTHFR	236250	U09806	1p36.3
		Dihydrofolate reductase/DHFR	126060	J00140	5q11.2-q13.2
		5,10-methylenetetrahydrofolate dehydrogenase, 5,10-			
		methylenetetrahydrofolate cyclohydrolase, 10-			
		formyltetrahydrofolate synthetase/MTHFD1	172460	NM_005956	14q24
		5,10-methylenetetrahydrofolate synthetase (5-formyltetrahydrofolate cyclo-ligase)/MTHFS	604197	NM_006441	Chr. 15
		phosphoribosylglycinamide formyltransferase,			
		phosphoribosylglycinamide synthetase,			
		phosphoribosylaminoimidazole	138440	NM_000819	21q22.1
		folate hydrolase 1/FOH1	600934	NP_004467	11q14
		6-pyruvoyl tetrahydrobiopterin synthase/PTPS	261640	Q03393	1q22.3-q23.3
		serine hydroxymethyltransferase 1 (soluble)/SHMT1	182144	NM_004169	17p11.2
		serine hydroxymethyltransferase 2 (mitochondrial)/SHMT2	138450	NM_005412	12q13
		Glycine aminotransferase/glycine cleavage T protein/GAT	238310	NM_000481	3p21.2-p21.1
		5-methyltetrahydrofolate-homocysteine methyltransferase/methionine	156570	NM_000254	1q43

Phase II Drug Metabolism (conjugation and catabolism)		glutamate formiminotransferase/dihydrofolate synthetase	229100	*****	*****
	Methylation	catechol-O-methyltransferase/COMT	116790	NM_000754	22q11.2
		phenylethanolamine N-methyltransferase/PNMT	171190	NM_002686	17q21-q22
		nicotinamide N-methyltransferase/NNMT	600008	NM_006169	11q23.1
	Carbon Unit Activation for Acetyl-CoA	Thiopurine methyltransferase (6-mercaptopurine detoxification)	187680	U12387	6p22.3
		pyruvate dehydrogenase E1-alpha subunit/PDHA1	312170	L48690	Xp22.2-p22.1
		pyruvate dehydrogenase (lipoamide) beta/PDHB	179060	NM_000925	3p13-q23
		pyruvate dehydrogenase complex, lipoyl-containing component X/E3-binding protein/PDX1	245349	NM_003477	11p13
	Acylation	pyruvate dehydrogenase complex E3 subunit/DLD	246900	NM_000108	7q31-q32
		sterol-O-acyl transferase 1/SOAT1	102642	L21934	1q25
		sterol-O-acyl transferase 2/SOAT2	601311	*****	chr. 12
		N-acetyltransferase 1/arylamine acetylase 1/NAT1	108345	NM_000662	8p23.1-p21.3
		N-acetyltransferase 2/arylamine acetylase 2/NAT2	243400	NM_000015	8p23.1-p21.3
		cystathionine-beta-synthase/CBS	236200	NM_000071	21q22.3

Glutathione Synthesis	cystathionase/cystathionine gamma-lyase/CTH	219500	NM_001902	Chr.16
	glutamate-cysteine ligase (gamma-glutamyl/cysteine synthetase), catalytic (72.8kD)/GLCLC	230450	NM_001498	6p12
	glutamate-cysteine ligase (gamma-glutamyl/cysteine synthetase), regulatory (30.8kD)/GLCLR	601176	NM_002061	1p22.1
	glutathione synthetase/GSS	601002	NM_000178	20q11.2
	Glutathione-S-transferase 6	138391	*****	*****
Glutathione Transferase	Glutathione-S-transferase, alpha 1/GSTA1	138359	L13269	6p12.2
	Glutathione-S-transferase, alpha 2/GSTA2	138360	M15872	6p12.2
	Glutathione-S-transferase, kappa 1/GSTK1	602321	*****	*****
	Glutathione-S-transferase 1/MGST1 (microsomal)	138330	AH003674	Chr.12
	Glutathione-S-transferase 2/MGST2 (microsomal)	601733	NM_002413	4q28-q31
	Glutathione-S-transferase, mu 1-like/GSTM1L	138270	*****	Chr. 3
	Glutathione-S-transferase, mu 1/GSTM1	138350	J03817	1p13.3
	Glutathione-S-transferase, mu 2/GSTM2 (muscle)	138380	NM_000848	1p13.3
	Glutathione-S-transferase, mu 3/GSTM3 (brain)	138390	NM_000849	1p13.3
	Glutathione-S-transferase, mu 4/GSTM4	138333	NM_000850	1p13.3

	Glutathione-S-transferase, mu 5/GSTM5 (brain/lung)	138385	NM_000851	1p13.3
	Glutathione-S-transferase, pi/GSTP1	134660	NM_000852	11q13
	Glutathione-S-transferase, theta 1/GSTT1	600436	NM_000853	22q11.2
	Glutathione-S-transferase, theta 2/GSTT2	600437	NM_000854	22q11.3
	Glutathione-S-transferase, zeta 1/maleylacetoacetate isomerase/MAAI/GSTZ1	603758	NM_001513	14q24.3
	Gamma-glutamyltranspeptidase 1/GGT1	231950	J04131	22q11.1-q11.2
	Gamma-glutamyltranspeptidase 2/GGT2	137181	AH002728	22q11.1
	Gamma-glutamyltransferase-like activity 1/GGTLA1	137168	NM_004121	*****
	paraoxonase 1/PON1 (arylesterase)	168820	AH004193	7q21.3
	paraoxonase 2/PON2	602447	L48513	7q21.3
	paraoxonase 3/PON3	602720	L48516	7q21.4
	esterase C/ESC (acetyl esterase)	133270	*****	*****
	esterase A4/ESA4	133220	*****	11q13-q22
	esterase B/buteryl esterase/ESB (erythrocyte)	133260	*****	*****
	esterase B3/ESB3	133290	*****	Chr.16
	esterase A5/A7/acetyl esterase/ESA5/ESA7 (brain)	133230	*****	*****
	acetylcholinesterase/ACHE	100740	M55040	7q22

Hydratases and Lyases	butyrylcholinesterase 1/serum cholinesterase 1/BCHE1	177400	NM_0000553q26.1-q26.2	
	butyrylcholinesterase 2/serum cholinesterase 2/BCHE2	177500	*****	2q33-q35
	egaseyn/esterase 22	129905	AF177775	*****
	neuropathy target esterase/NTE	603197	NM_006702	19p
	carboxylesterase 1/serine esterase/CES1 (hepatic)	114835	NM_001266	16q13-q22.1
	arylacetamide deacetylase/AADAC	600338	NM_001086	3q21.3-q25.2
	acyl-CoA thioester hydrolase 1, long chain/acyl-CoA thioesterase 1/ACT1	602586	*****	*****
	acyl-CoA thioester hydrolase 2, long chain/acyl-CoA thioesterase 2/ACT2	602587	*****	*****
	esterase D/ESD	133280	M13450	13q14.11
	hydroxyacyl glutathione hydrolase; glyoxalase 2/HAGH	138760	NM_005326	16p13
Thioesterase	esterase D/S-formylglutathion hydrolase/ESC (thioesterase)	133280	M13450	13q14.11
	aminoacylase 1/ACY1	104620	NM_000666	3p21.1
	aminoacylase 2/ACY2/aspartoacylase (Canavan disease)/ASPA	271900	NM_000049	17pter-p13
	fatty acid amide hydrolase/FAAH	602935	NM_001441	1p34-p35
Amidase	epoxide hydrolase 1/EPHX1 (microsomal)	132810	NM_000120	1p11-qter
	epoxide hydrolase 2/EPHX2	132811	*****	8p21-p12
Proteases	bleomycin hydrolase/BLMH	602403	NM_000386	17q11.2

Transporters	Multidrug resistance protein MDR3/P-glycoprotein 3/PGY3	602347	X06181	7q21.1
	Familial intrahepatic cholestasis 1, (progressive, Byler disease and benign recurrent) /FIC1	602397	NM_005603	18q21
	Bile salt export pump/BSEP	603201	NM_003742	2q24
	Microsomal triglyceride transfer protein large subunit/MTP	157147	NM_000253	4q22-q24
	Solute carrier family 6, member 6/SLC6A6 (taurine)	186854	U16120	3p25-q24
	Solute carrier family 10, member 1/SLC10A1 (taurocholate)	182396	NM_003049	chr. 14
	Solute carrier family 10, member 2/SLC10A2 (taurocholate)	601295	NM_000452	13q33
	Solute carrier family 13, member 2/SLC13A2 (dicarboxylic acids)	604148	NM_003984	17p11.1-q11.1
	Solute carrier family 19, member 1/SLC19A1 (reduced folate)	600424	U19720	21q22.3
	Solute carrier family 21, member 3/SLC21A3 (organic anion)	602883	NM_005075	12p12
	Solute carrier family 22, member 1/SLC22A2 (organic cation)	602607	NM_003058	6q26
	multidrug resistance protein MDR1	171050	X96395	7q21.1
	multidrug resistance associated protein MRP2/CMOAT	601107	NM_000392	10q24
	multidrug resistance protein MDR3/P-glycoprotein 3/PGY3	602347	X06181	7q21.1

Bile Salt Synthesis	Bile acid Coenzyme A: amino acid N-acyltransferase (glycine N-choloyltransferase)/BAAT	602938	NM_001701	9q22.3
	cytochrome P450, subfamily XLVI (cholesterol 24-hydroxylase)/CYP46	604087	NM_006668	14q32.1
	cytochrome P450, subfamily VIIA (cholesterol 7- α -hydroxylase), polypeptide 1/CYP7A1	118455	M89803	8q11-q12
	cytochrome P450, subfamily VIIB (oxysterol 7- α -hydroxylase), polypeptide 1/CYP7B1	603711	AF029403	8q21.3
Canalicular Uptake and Concentration	ATPase, Na ⁺ /K ⁺ transporting, alpha 1 polypeptide/ATPIA1	182310	NM_000701	1p13-p11
	ATPase, Na ⁺ /K ⁺ transporting, alpha 1 polypeptide-like/ATPIA1L	182360	NM_001676	13q12.1-q12.3
	ATPase, Na ⁺ /K ⁺ transporting, alpha 2 polypeptide/ATPIA2	182340	NM_000702	1q21-q23
	ATPase, Na ⁺ /K ⁺ transporting, beta 1 polypeptide/ATPIB1	182330	NM_001677	1q22-q25
	ATPase, Na ⁺ /K ⁺ transporting, beta 2 polypeptide/ATPIB2	182331	X16645	17p
	ATPase, Na ⁺ /K ⁺ transporting, beta 3 polypeptide/ATPIB3	601867	NM_001679	3q22-q23
	solute carrier family 4, bicarbonate/chloride anion exchanger, member 1/SLC4A1	109270	NM_000342	17q21-q22
	solute carrier family 4, sodium bicarbonate cotransporter, member 4/SLC4A4	603345	NM_003759	4q21
Bile				

Concentration	solute carrier family 4, sodium bicarbonate cotransporter, member 5/SLC4A5	603318	NM_003788	4q21
	Solute carrier family 9, member A2/SLC9A2 (sodium/hydrogen ion)	600530	NM_003048	2q11.2
	Solute carrier family 9, member A3/SLC9A3 (sodium/hydrogen ion)	182307	*****	5p15.3
	chloride channel 5/CLCN5	300008	NM_000084	Xp11.22
	chloride channel, calcium activated, family member 1/CLCA1	603906	NM_001285	1p31-p22
	chloride channel, calcium activated, family member 2/CLCA2	604003	NM_006536	*****
	cystic fibrosis transmembrane conductance regulator/CFTR	602421	NM_000492	7q31.2
	aquaporin 1/AQP1	107776	NM_000385	7p14
	aquaporin 3/AQP3	600170	NM_004925	9p13
	Cholecystokinin/CCK	118440	L00354	3pter-p21
Bile Secretion	Cholecystokinin A receptor/CCKAR	118444	L13605	4p15.2-p15.1
	Cholecystokinin B receptor/CCKBR	118445	L08112	11p15.5-p15
	Cytoplasmic cysteine conjugate-beta-lyase/glutamine transaminase 1/CCBL1	600547	NM_004059	Chr.9
	renal microsomal dipeptidase/DPEP1	179780	NM_004413	16q24.3
	alanyl (microsomal) aminopeptidase/aminopeptidase M/ANPEP	151530	NM_001150	15q25-q26

Hydratases and Lyases	Galectosamine (N-acetyl)-D-sulfate sulfatase (Morquio syndrome)/CA1C	253000	NM_00051 2	16q24.3
	Iduronate-2-sulfatase (Hunter syndrome)/IDS	309900	NM_00020 2	Xq28
	Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7	22q13.31- qter
	Arylsulfatase B/steroid sulfatase/ARSB	253200	NM_00004 6	5q11-q13
	Arylsulfatase C, isozyme s/steroid sulfatase/ARCS1	308100	NM_00035 1	Xp22.32
	Arylsulfatase D/steroid sulfatase/ARSD	300002	*****	Xp22.3
	Arylsulfatase E/steroid sulfatase/ARSE	300180	NM_00004 7	Xp22.3
	Arylsulfatase F/steroid sulfatase/ARSF	300003	NM_00404 2	Xp22.3
	glucuronidase, beta/GUSB	253220	NM_00018 1	7q21.11
	renal transport of beta-amino acids/AABT	109660	*****	Chr.21
Uptake and Transport	Solute carrier family 3 member 1/SLC3A1 (aa transporter)	104614	*****	2p16.3
	Solute carrier family 5 member 2/SLC5A5 (Na/glucose transporter)	182381	A56765	16p11.2
	Solute carrier family 6, member 6/SLC6A6 (taurine)	186854	U16120	3p25-q24
	Solute carrier family 7, member 9/SLC7A9 (neutral AA)	604144	*****	19q13.1
	Solute carrier family 13, member 2/SLC13A2 (dicarboxylic acids)	604148	NM_00398 4	17p11.1- q11.1

Renal Tubular Uptake and Concentration	Transporters	solute carrier family 17 (sodium phosphate), member 1/SLC17A1	182308	NM_005074	6p23-p21.3
		Solute carrier family 22, member 1/SLC22A2 (organic cation)	602607	NM_003058	6q26
		Solute carrier family 22, member 1-like/SLC22A1L (organic cation)	602631	AF037064	11p15.5
		Solute carrier family 22, member 4/SLC22A4 (organic cation)	604190	NM_003059	Chr. 5
		Solute carrier family 22, member 5/SLC22A5 (carnitine)	603377	NM_003060	5q33.1
		Solute carrier family 34, member 1/SLC34A1 (sodium phosphate)	182309	NM_003052	5q35
		H ⁺ -ATPase beta 1 subunit /ATP6B1	267300	AH007312	2cen-q13
		solute carrier family 4, sodium bicarbonate cotransporter, member 4/SLC4A4	603345	NM_003759	4q21
		solute carrier family 4, sodium bicarbonate cotransporter, member 5/SLC4A5	603318	NM_003788	4q21
		carbonic anhydrase II/CA2	259730	NM_000067	8q22
Acidosis		carbonic anhydrase IV/CA4	114760	NM_000717	17q23
		carbonic anhydrase XII/CA12	603263	AF051882	15q22
		solute carrier family 4, bicarbonate/chloride anion exchanger, member 1/SLC4A1	109270	NM_000342	17q21-q22
		Solute carrier family 9, member A1/SLC9A1 (sodium/hydrogen ion)	107310	M81768	1p36.1-p35

	Solute carrier family 9, member A2/SLC9A2 (sodium/hydrogen ion)	600530	NM_003048	2q11.2
	Solute carrier family 9, member A3/SLC9A3 (sodium/hydrogen ion)	182307	*****	5p15.3
Lithosis	Solute carrier family 13, member 2/SLC13A2 (dicarboxylic acids)	604148	NM_003984	17p11.1-q11.1
Sodium Tolerance	3'(2'), 5'-bisphosphate nucleotidase 1/BPNT	604053	NM_006085	*****
	chloride channel 5/CLCN5	300008	NM_000084	Xp11.22
	chloride channel Ka, kidney/CLCNKA	602024	NM_004070	1p36
	chloride channel Kb, kidney/CLCNKB	602023	NM_000085	1p36
	solute carrier family 12 (sodium/potassium/chloride transporters), member 1/SLC12A1	600839	NM_000338	15q15-q21.1
	solute carrier family 12 (sodium/potassium/chloride transporters), member 2/SLC12A2	600840	NM_001046	5q23.3
	solute carrier family 12 (sodium/chloride transporters), member 3/SLC12A3	600968	NM_000339	16q13
	ATPase, Na+/K+ transporting, alpha 1 polypeptide/ATP1A1	182310	NM_000701	1p13-p11
	ATPase, Na+/K+ transporting, alpha 1 polypeptide-like/ATP1A1L	182360	NM_001676	13q12.1-q12.3
Urine Concentration	ATPase, Na+/K+ transporting, alpha 2 polypeptide/ATP1A2	182340	NM_000702	1q21-q23

	ATPase, Na+/K+ transporting, beta 1 polypeptide/ATP1B1	182330	NM_001677	1q22-q25
	ATPase, Na+/K+ transporting, beta 2 polypeptide/ATP1B2	182331	X16645	17p
	ATPase, Na+/K+ transporting, beta 3 polypeptide/ATP1B3	601867	NM_001679	3q22-q23
	arginine vasopressin receptor 2 (nephrogenic diabetes insipidus)/AVPR2	304800	NM_000054	Xq28
	aquaporin 1/AQP1	107776	NM_000385	7p14
	aquaporin 2/AQP2	107777	NM_000486	12q13
	aquaporin 3/AQP3	600170	NM_004925	9p13
	aquaporin 6/AQP6	601383	NM_001652	12q13
	Superoxide Dismutase 1/SOD1 (soluble)	147450	NM_000454	21q22.1
	Superoxide Dismutase 2/SOD2 (mitochondrial)	147460	X65965	6q25.3
Superoxide Dismutase	Superoxide Dismutase 3/SOD3 (extracellular)	185490	NM_003102	4pter-q21
	aldehyde dehydrogenase 1/ALDH1 (liver cytosol)	100640	AH002598	9q21
	aldehyde dehydrogenase 2/ALDH2 (liver mitochondria)	100650	K03001	12q24.2
	aldehyde dehydrogenase 3/acetaldehyde dehydrogenase 1/ALDH2 (cytosol)	100660	M74542	17p11.2

Metabolism of Reactive Oxygen and Nitrogen Species	Protection from Reactive Oxygen and Nitrogen Species	Aldehyde Dehydrogenase	5/acetalddehyde aldehyde dehydrogenase 5, member A1/succinic semialdehyde dehydrogenase/ALDH5A1	100670	NM_00069 2	9p13
			6/acetalddehyde aldehyde dehydrogenase 6, member A1/succinic semialdehyde dehydrogenase/ALDH6A1	271980	NM_00108 0	6p22
			7/acetalddehyde aldehyde dehydrogenase 7, member A1/succinic semialdehyde dehydrogenase/ALDH7A1	600463	NM_00069 3	15q26
			8/acetalddehyde aldehyde dehydrogenase 8/ALDH8	600466	NM_00069 4	11q13
			9/acetalddehyde aldehyde dehydrogenase 9/g- aminobutyraldehyde dehydrogenase/ALDH9	601917	NM_00069 5	chr. 11
			10/acetalddehyde aldehyde dehydrogenase 10/ALDH10	602733	NM_00069 6	1q22-q23
			11/acetalddehyde aldehyde dehydrogenase 11/ALDH11	270200	NM_00038 2	17p11.2
			12/acetalddehyde aldehyde dehydrogenase 12/ALDH12	602841	NM_00115 9	2q33
			13/acetalddehyde aldehyde dehydrogenase 13/ALDH13	230450	NM_00149 8	6p12
			14/acetalddehyde aldehyde dehydrogenase 14/ALDH14	601176	NM_00206 1	1p22.1
Glutathione	Glutathione	Glutathione	glutathione synthetase/GSS	601002	NM_00017 8	20q11.2
			glutathione peroxidase/GPX1	138320	M21304	3p21.3
			glutathione peroxidase GPX2	138319	X68314	14q24.1

	glutathione peroxidase GPX3	138321	X58295	5q32-q33.1
	glutathione peroxidase GPX4	138322	X71973	19p13.3
	glutathione peroxidase GPX5	603435	AJ005277	*****
	glutathione reductase	138300	X15722	8p21.1
Metallothioneins	metallothionein 1A/MT1A	156350	NM_005953	16q13
	metallothionein 1B	56349	AH001510	16q13
	metallothionein 1E	156351	M10942	16q13
	metallothionein 1F	156352	M10943	16q13
	metallothionein 1G	156353	J03910	16q13
	metallothionein 2A/MT2A	156360	NM_005953	16q13
	metallothionein 3	139255	NM_005954	16q13
	glucose-6-phosphate dehydrogenase/G6PD (mitochondrial)	305900	NM_000402	Xq28
Miscellaneous	8-oxoguanine DNA glycosylase/CGGI	601982	NM_002542	3p26.2
	Peptide methionine sulfoxide reductase/MSRA	601250	*****	*****
	succinate dehydrogenase complex, subunit C, integral membrane protein/SDHC	602413	NM_003001	1q21
	phospholipase A2 group IB/PLA2G1B	172410	NM_000928	12q23-q24.1
	lipoprotein, Lp(a)/LPA	152200	NM_005557	6q27
	Catalase/CAT	115500	NM_001752	11p13

	thioredoxin-dependent peroxide reductase/TDPX1	600538	NM_005809	13q12
IgE Production	interleukin 4 receptor/IL4R	147781	X52425	6p12.1-p11.2
	interferon gamma/IFNG	147570	L07633	12q14
Mast Cell Proliferation	mast cell growth factor/MGF	184745	NM_003994	12q22
	interleukin 9 receptor/IL9R	300007	M84747	Xq28
	interleukin 3 receptor/IL3R)	308385	M74782	Xp22.3
Degranulation of Mast Cells	mast cell IgE receptor alpha polypeptide/FCER1A	147140	*****	1q23
	mast cell IgE receptor beta polypeptide/FCER1B	147138	NM_000139	11q13
	mast cell IgE receptor beta polypeptide/FCER1G	147139	NM_004106	1q23
	SH2-containing inositol 5-phosphatase/SHIP	601582	U57650	2q36-q37
	secretory granule proteoglycan peptide core/PRG1	177040	J03223	10q22.1
	Histidine Decarboxylase	142704	M60445	15q21-q22
Histamine	Histamine receptor H1	600167	AF026261	3p21-p14
	Histamine receptor H2	142703	M64799	*****
	Histamine N-methyltransferase	*****	D16224	chr. 2
	Amine oxidase (copper-containing) 2/AOC2	602268	D88213	17q21
	Amine oxidase (copper-containing) 3/AOC3	603735	AF054985	17q21
	aromatic L-Amino Acid Decarboxylase/AADC	107930	M76180	7p11

tryptophan hydroxylase/TPH	191060	X52836	11p15.3-p14
14-3-3 protein ETA	113508	X78138	22q12
14-3-3 protein ZETA	601288	M86400	2p25.2-p25.1
14-3-3 protein BETA	601289	X57346	20q13.1
14-3-3 protein SIGMA	601290	X57348	*****
serotonin 5-HT receptors 5-HT1A, G protein-coupled	109760	X57829	5q11.2-q13
serotonin 5-HT receptors 5-HT1B, G protein-coupled	182131	M81590	6q13
serotonin 5-HT receptors 5-HT1C, G protein-coupled	312861	U49516	Xq24
serotonin 5-HT receptors 5-HT1D, G protein-coupled	182133	M81590	1p36.3-p34.3
serotonin 5-HT receptors 5-HT1E, G protein-coupled	182132	M91467	6q14-q15
serotonin 5-HT receptors 5-HT1F, G protein-coupled	182134	L05597	3p12
serotonin 5-HT receptors 5-HT2A, G protein-coupled	182135	D87030	13q14-q21
serotonin 5-HT receptors 5-HT2B, G protein-coupled	601122	X77307	2q36.3-q37.1
serotonin 5-HT receptors 5-HT2C, G protein-coupled	312861	U49516	Xq24
serotonin transporter	182138	X70697	17q11.1-q12
monoamine oxidase A/ MAOA	309850	M69226	Xp11.23
monoamine oxidase B MAOB	309860	M69177	Xp11.23
serotonin N-Acetyltransferase/SNAT	600950	U40347	17q25
tryptophan 2,3-dioxygenase/TDO2	191070	NM_005651	4q31-q32

Serotonin

Neutrophil and Eosinophil Chemotaxis	eotaxin precursor/small inducible cytokine, family A, member monocyte-derived-neutrophil chemotactic factor/interleukin 8/IL8	601156	U46572	7q21.1-q21.2
Proteases	tryptase alpha/TPS1	146930	M26383	4q12-q13
	tryptase beta/TPS2	191080	NM_003293	Chr.16
	chymase 1, mast cell/CMA1	191081	NM_003294	Chr.16
		118938	NM_001836	14q11.2
Release of Membrane Lipids (common to PAF, leukotriene, and prostaglandin pathways)	phospholipase A2 group IIA/PLA2G2A	172411	NM_000300	1p35
	phospholipase A2 group IB/PLA2G1B	172410	NM_000928	12q23-q24.1
	phospholipase A2 group X/PLA2G10	603603	*****	16p13.1-p12
	phospholipase A2 group IVA/PLA2G4A	600522	U08374	1q25
	phospholipase A2 group VI/PLA2G6	603604	AF064594	22q13.1
	phospholipase A2 group IVC/PLA2G4C	603602	*****	chr. 19
	phospholipase A2 group V/PLA2G5	601192	NM_000929	1p36-p34
	phospholipase C beta 3	600230	U26425	11q13
	lysosomal acid lipase	278000	NM_000235	10q24-q25
	CDP-choline:alkylacetyl glycerol cholinephosphotransferase	*****	*****	*****
Platelet Activation	platelet activating factor receptor/PTAFR	173393	M88177	1p35-p34.3
	platelet activating factor acetylhydrolase 1/PAFAH1	601690	NM_005084	6p21.2-p12

Platelet Activating Factor (PAF)	platelet activating factor acetylhydrolase, isoform 1B, alpha	601545	NM_000430	17p13.3
	platelet activating factor acetylhydrolase, isoform 1B, beta	602508	NM_002572	11q23
	platelet activating factor acetylhydrolase, isoform 1B, gamma	603074	NM_002573	19q13.1
	platelet activating factor acetylhydrolase 2/PAFAH2	602344	NM_000437	*****
	arachidonate 5-lipoxygenase/ALOX5	152390	NM_000698	Chr.10
Leukotriene	arachidonate 5-lipoxygenase-activating protein/FLAP/ALOX5AP	603700	NM_001629	13q12
	leukotriene A4 hydrolase/LTA4H	151570	NM_000895	12q22
	leukotriene C4 synthase/LTC4S	246530	NM_000897	5q35
	Gamma-glutamyltranspeptidase 1/GGT1	231950	J04131	22q11.1-q11.2
	Gamma-glutamyltranspeptidase 2/GGT2	137181	AH002728	22q11.1
	Gamma-glutamyltransferase-like activity 1/GGTLA1	137168	NM_004121	*****
	renal microsomal dipeptidase/DPEP1	179780	NM_004413	16q24.3
	cysteinyl leukotriene receptor 1/CYSLT1	300201	NM_006639	Xq13-q21
	leukotriene b4 receptor (chemokine receptor-like 1)/LTB4R	601531	NM_000752	14q11.2-q12

Prostaglandins	prostaglandin endoperoxide synthetase 1/COX1/PTGS1	176805	AH001520	9q32-q33.3
	prostaglandin endoperoxide synthetase 2/COX2/PTGS2	600262	NM_000963	1q25.2-q25.3
	thromboxane A synthase 1/TBXAS1	274180	SEG_D3461	7q34
	prostaglandin D2 synthase	602598	M61900	*****
	prostaglandin I2 synthase/prostacyclin synthase/PTGIS	601699	SEG_D8339	20q13
	prostaglandin E receptor 1, EP1 subtype/PTGER1	176802	NM_000955	19p13.1
	prostaglandin E receptor 2, EP2 subtype/PTGER2	176804	*****	5p13.1
	prostaglandin E receptor 3, EP3 subtype/PTGER3	176806	NM_000957	1p31.2
	prostaglandin E receptor 4, EP4 subtype/PTGER4	601586	NM_000958	5p13.1
	prostaglandin F receptor/PTGFR	600563	L24470	1p31.1
	prostaglandin F2 receptor negative regulator/PTGFRN	601204	U26664	1p13.1-q21.3
	prostaglandin I2 receptor/PTGIR/prostacyclin receptor	600022	SEG_HUM1	19q13.3
	15-hydroxyprostaglandin dehydrogenase/HPGD	601688	NM_000860	4q34-q35
	aldo-keto reductase family 1, member C2/AKR1C2	600450	NM_001353	10p15-p14
	myeloperoxidase/MPO	254600	J02694	17q23.1
	eosinophil peroxidase/EPX	131399	NM_000502	*****

Mast Cell
and T-Cell
Response

Drug Activation	calreticulin/CALR	109091	CALR	19p13.2
	calnexin/CANX	114217	L18887	5q35
	ceruloplasmin (ferroxidase)/CP	117700	NM_000096	3q21-q24
Antigen Presentation	MHC class II transactivator/MHC2TA	600005	NM_000246	16p13
	MHC class II HLA DR-alpha chain/HLA-DRA	142860	X83114	6p21.3
	MHC class II HLA DR-beta chain/HLA-DRB	142857	M11161	6p21.3
	MHC class II HLA DP-alpha chain/HLA-DPA	142880	M23905	6p21.3
	MHC class II HLA DP-beta chain/HLA-DPB	142858	AH002893	6p21.3
	MHC class II HLA DM-alpha chain/HLA-DMA	142855	NM_006120	6p21.3
	MHC class II HLA DM-beta chain/HLA-DMB	142856	NM_002118	6p21.3
	MHC class II HLA DQ-alpha chain/HLA-DQA	146880	M11124	6p21.3
	MHC class II HLA DQ-beta chain/HLA-DQB	*****	M24364	6p21.3
	MHC class II HLA DN-alpha chain/HLA-DNA	142930	X02882	6p21.3
	MHC class II HLA DO-beta chain/HLA-DOB	600629	NM_002120	6p21.3
	MHC class II antigen gamma chain/CD74	142790	K01144	5q32

	antigen peptide transporter 1/MHC 1/TAP1	170260	NM_000593	6p21.3
	antigen peptide transporter 2/MHC 2/TAP2	170261	NM_000544	6p21.3
T-Cell Receptor	T-cell antigen receptor, alpha subunit/TCRA	186880	Z24457	14q11.2
	T-cell antigen receptor, beta subunit/TCRB	186930	AF011643	7q35
	T-cell antigen receptor, gamma subunit/TCRG	186970	M17325	7p15-p14
	T-cell antigen receptor, delta subunit/TCRD	186810	L36384	14q11.2
	thymocyte antigen receptor complex CD3G, gamma polypeptide (TiT3 complex)/CD3G	186740	NM_000073	11q23
	thymocyte antigen receptor complex CD3D, delta polypeptide (TiT3 complex)/CD3D	186790	NM_000073	11q23
	thymocyte antigen receptor complex CD3E, epsilon polypeptide (TiT3 complex)/CD3E	186830	NM_000073	11q23
	thymocyte antigen receptor complex CD3Z, zeta polypeptide (TiT3 complex)/CD3Z	186780	NM_000073	1q22-q23
	ataxia telangiectasia mutated (includes complementation groups A, C and D)/ATM	208900	NM_000051	11q22.3
	recombination activating gene 1/RAG1	179615	NM_000448	11p13

T-Cell Receptor Rearrangement	recombination activating gene		179616	M94633	11p13
	α/β	γ/δ			
T-Cell Receptor Rearrangement	interleukin 7 receptor/IL7R		146661	NM_002185	5p13
	v-myb avian myeloblastosis viral oncogene homolog/MYB		189990	NM_005375	6q22
	core binding factor, alpha 1 subunit/CBFA1		600211	AH005498	6p21
	core-binding factor, beta subunit/PEBP2B/CBFB		121360	L20298	16q22
	ligase I, DNA, ATP-dependent/LIG1		126391	NM_000234	19q13.2-q13.3
	ligase IV, DNA, ATP-dependent/LIG4		601837	NM_002312	13q22-q34
	X-ray repair, complementing defect in Chinese hamster/Ku antigen, 80 kD/KU80/XRCC5		194364	*****	2q35
	thyroid autoantigen, 70 kD/KU70/G22P1		152690	NM_001469	22q11-q13
	T-cell antigen T4/CD4		186940	X87579	12pter-p12
	T-cell antigen CD8, alpha polypeptide (p32)/CD8A		186910	NM_001768	2p12
	T-cell antigen CD8, beta polypeptide/CD8B		186730	AH003859	2p12
	T-cell antigen CD28 (Tp44)/CD28		186760	NM_006139	2q33-q34
	cytotoxic T-lymphocyte-associated 4/CTLA4		123890	L15006	2q33

CD80 antigen (CD28 antigen ligand 1, B7-1 antigen)/CD80	112203	NM_005191	3q21
CD86 antigen (CD28 antigen ligand 2, B7-2 antigen)/CD86	601020	NM_006889	3q21
T cell receptor-associated protein tyrosine kinase ZAP-70/ZAP70	176947	S69911	2q12
leukocyte common antigen CD45	151460	M23492	1q31-q32
nuclear factor of activated T-cells, cytoplasmic 1/NFATC1	600489	NM_006162	18q23
nuclear factor of activated T-cells, cytoplasmic 2/NFATC2	600490	*****	20q13.2-q13.3
nuclear factor of activated T-cells, cytoplasmic 3/NFATC3	602698	L41066	16q13-q24
nuclear factor of activated T-cells, cytoplasmic 4/NFATC4	602699	L41067	*****
interleukin 2 receptor alpha/IL2RA	147730	X01057	10p15-p14
interleukin 2 receptor beta/IL2RB	146710	M26062	22q11.2-q13
interleukin 2 receptor gamma/IL2RG	308380	D11086	Xq13
interleukin 6 receptor/IL6R	147880	X12830	1q21
interleukin 9 receptor/IL9R	300007	M84747	Xq28
interleukin receptor 13 alpha/IL13RA1	300119	S80963	Chr.X
interleukin receptor 13 alpha2/IL13RA2	300130	X95302	Xq24
interleukin 15 receptor alpha/IL15RA	601070	U31628	10p15-p14
transforming growth factor/TGFB1	190180	M60315	19q13.1-q13
transforming growth factor/TGFB2	190220	M19154	1q41
transforming growth factor/TGFB3	190230	X14149	14q24
tumor necrosis factor beta/TNFB/lymp	153440	NM_000595	6p21.3

T-Cell Expansion

**Immune
Response**
(*additional
genes in
Immunology*)

tumor necrosis factor ligand superfamily, member 6/TNFSF6	134638	NM_00063 9	1q23
tumor necrosis factor receptor superfamily, member 6/TNFRSF6	134637	NM_00004 3	10q24.1
caspase 10, apoptosis-related cysteine protease/CASP10	601762	NM_00123 0	2q33-q34
B-cell antigen CD20/B-lymphocyte differentiation antigen B1/CD20	112210	AH003353	11q13
B-cell antigen CD72/CD72	107272	NM_00178 2	9p
natural resistance-associated macrophage protein 1/NRAMP1/solute carrier family 11, member 1/SLC11A2	600266	AH002806	2q35
natural resistance-associated macrophage protein 2/NRAMP2/solute carrier family 11, member 2/SLC11A2	600523	AB015355	12q13
T-lymphocyte antigen CDW52 (CAMPATH-1 antigen)/CDW52	114280	NM_00180 3	*****
B-cell antigen CD22/CD22	107266	NM_00177 1	19q13.1
B-cell antigen CD24/CD24	600074	X69397	6q21
leukocyte antigen CD156/disintegrin and metalloprotease domain 8/ADAM8/CD156	602267	NM_00110 9	10q26.3
platelet antigen CD151/platelet- endothelial cell tetraspan antigen 3/PETA3/CD151	602243	NM_00435 7	11p15.5

Receptors

	IIA for Fc fragment of IgG/FCGR2A/CD32	146790	NM_004001	1q21-q23
	activated leucocyte cell adhesion molecule/CD6 ligand/ALCAM	601662	NM_001627	3q13.1-q13.2
	lymphocyte antigen CD79A/immunoglobulin-associated alpha/CD79A	112205	NM_001783	19q13.2
	lymphocyte antigen CD79B/immunoglobulin-associated beta/CD79B	147245	L27587	17q23
Signalling	regulator of G-protein signalling 1/RGS1	600323	NM_002922	1q31
Immunoglobulin Light Chains	immunoglobulin K light chain constant region locus/IGKC	147200	*****	2p12
	immunoglobulin K light chain variable region locus/IGKV	146980	K01322	2p12
	immunoglobulin K light chain joining region locus/IGKJ	146970	*****	2p12
	immunoglobulin L light chain constant region locus/IGLC1	147220	NM_006146	22q11.2
	immunoglobulin L light chain joining region locus/IGLJ	147230	NM_006146	22q11.2
	immunoglobulin L light chain variable region locus/IGLJ	147240	NM_006146	22q11.2
	immunoglobulin A heavy chain constant region locus 1/IGHA1	146900	*****	14q32.33
	immunoglobulin A heavy chain constant region locus 2/IGHA2	147000	*****	14q32.33

Immunoglobulin Heavy Chains	immunoglobulin D heavy chain constant region locus/IGHD	147170	*****	14q32.33
	immunoglobulin E heavy chain constant region locus/IGHE	147180	*****	14q32.33
	immunoglobulin G heavy chain constant region locus 1/IGHG1	147100	*****	14q32.33
	immunoglobulin G heavy chain constant region locus 2/IGHG2	147110	*****	14q32.33
	immunoglobulin G heavy chain constant region locus 3/IGHG3	147120	*****	14q32.33
	immunoglobulin G heavy chain constant region locus 4/IGHG4	147130	*****	14q32.33
	immunoglobulin M heavy chain constant region locus/IGHM	147020	*****	14q32.33
	immunoglobulin heavy chain variable region locus 1/IGHV1	147070	X92279	14q32.33
	immunoglobulin heavy chain variable region locus 2/IGHV2	600949	*****	16p11
	immunoglobulin heavy chain diversity region locus 1/IGHDY1	146910	X97051	14q32.33
	immunoglobulin heavy chain diversity region locus 2/IGHDY2	146990	L25544	15q11-q12
	immunoglobulin heavy chain joining region locus/IGHJ	147010	*****	14q32.33
	recombination activating gene 1/RAG1	179615	NM_000448	11p13
	recombination activating gene 2/RAG2	179616	M94633	11p13

B-Cell Response	Immunoglobulin Gene Rearrangement	147183	L07872	9p13-p12
	immunoglobulin kappa J region recombination signal binding protein/RBPJK/IGKJRB1	147183	L07872	9p13-p12
	Bruton agammaglobulinemia tyrosine kinase/BTK	300300	NM_000061	Xq21.3-q22
	interleukin 7 receptor/IL7R	146661	NM_002185	5p13
	interferon-gamma receptor 1/IFNGR1	107470	NM_000416	6q23-q24
	interferon-gamma receptor 2/IFNGR2	147569	NM_005534	21q22.1-q22.2
	interleukin 4 receptor precursor/IL4R	147781	NM_000418	16p12.1-p11.2
	interleukin 4 receptor precursor/IL4R	147781	NM_000418	16p12.1-p11.2
	ligase I, DNA, ATP-dependent/LIG1	126391	NM_000234	19q13.2-q13.3
	ligase IV, DNA, ATP-dependent/LIG4	601837	NM_002312	13q22-q34
	X-ray repair, complementing defect in Chinese hamster/Ku antigen, 80 kD/KU80/XRCCC5	194364	*****	2q35
	thyroid autoantigen, 70 kD/KU70/G22P1	152690	NM_001469	22q11-q13
	nuclear factor kappa-B DNA binding subunit 1/NFKB1	164011	M58603	4q23-q24
	nuclear factor kappa-B DNA binding subunit 2/NFKB2	164012	NM_002502	10q24

Immunoglobulin Gene Transcription	nuclear factor kappa-B subunit 3/NFKB3	164014	Z22949	11q12-q13
	nuclear factor of kappa light chain gene enhancer in B cells, inhibitor alpha/NFKBIA	164008	*****	14q13
	nuclear factor of kappa light chain gene enhancer in B cells, inhibitor beta/NFKBIB	603258	NM_002503	8p11.2
	YY1 transcription factor/YY1	600013	NM_003403	14q
	immunoglobulin transcription factor 1/ITF1/transcription factor 3/TCF3	147141	*****	19p13.3
	immunoglobulin transcription factor 2/ITF2/transcription factor 4/TCF4	602272	NM_003199	18q21.1
	immunoglobulin mu binding protein 2/IGHMBP2	600502	NM_002180	11q13.2-q13.4
	transcription factor binding to IGHM enhancer 3/TFE3	314310	NM_006521	Xp11.22
	homeobox protein OCT1/POU domain transcription factor 2, class 1/POU2F1	164175	NM_002697	1q22-q23
	homeobox protein OCT2/POU domain transcription factor 2, class 2/POU2F2	164176	M22596	Chr.19
	POU domain, class 2, associating factor 1/POU2AF1	601206	NM_006235	11q23.1
	inhibitor of DNA binding 1, dominant negative helix-loop-helix protein/ID1	600349	NM_002165	20q11.1
	inhibitor of DNA binding 2, dominant negative helix-loop-helix protein/ID2	600386	NM_002166	2p25

Immunoglobulin Isotype Switching	B-cell antigen CD40/tumor necrosis factor receptor superfamily, member 5/CD40/TNFRSF5	109535	NM_001250	20q12-q13.2
	paired box gene 5/B-cell lineage-specific activator protein/BSAP/PAX5	167414	*****	9p13
	lymphocyte function-associated antigen, type 3/LFA3/LEU7/CD58	153420	NM_001779	1p13
	interleukin 10 receptor, alpha/IL10RA	146933	NM_001558	11q23.3
	lymphocyte antigen CD45/protein tyrosine phosphatase, receptor type, c polypeptide/PTPRC/CD45	151460	NM_002838	1q31-q32
	prostaglandin E receptor 1, EP1 subtype/PTGER1	176802	NM_000955	19p13.1
	prostaglandin E receptor 2, EP2 subtype/PTGER2	176804	*****	5p13.1
	prostaglandin E receptor 3, EP3 subtype/PTGER3	176806	NM_000957	1p31.2
	prostaglandin E receptor 4, EP4 subtype/PTGER4	601586	NM_000958	5p13.1
	interleukin 13 receptor, alpha 1/IL13RA1	300119	NM_001560	Chr.X
	interleukin receptor 13 alpha2/IL13A2	300130	X95302	Xq24
	interferon-gamma receptor 1/IFNGR1	107470	NM_000416	6q23-q24
	interferon-gamma receptor 2/IFNGR2	147569	NM_005534	21q22.1-q22.2
	interleukin 5 receptor alpha/IL5RA	147851	M96652	3p26-p24:

transforming growth factor, beta receptor I (activin A receptor type II- like kinase, 53kD)/TGFBRI	190181	NM_00461 2	9q33-q34
transforming growth factor, beta receptor II (70-80kD)/TGFBRI2	190182	NM_00324 2	3p22
transforming growth factor, beta receptor III (betaglycan, 300kD)/TGFBRI3	600742	NM_00324 3	1p33-p32
X-ray repair, complementing defect in Chinese hamster/Ku antigen, 80 kD/KU80/XRCC5	194364	*****	2q35
thyroid autoantigen, 70 kD/KU70/G22P1	152690	NM_00146 9	22q11-q13
granulocyte-macrophage colony stimulating factor 2/CSF2	138960	NM_00075 8	5q31.1
macrophage-specific colony- stimulating factor/CSF1	120420	AH005300	1p21-p13
granulocyte colony stimulating factor 3/CSF3	138970	NM_00075 9	17q11.2- q12
colony stimulating factor 1 receptor/CSFR1	164770	U63963	5q33.2- q33.3
granulocyte-macrophage colony stimulating factor 2 receptor, alpha, low-affinity/CSF2RA	306250	NM_00614 0	Xp22.32
granulocyte-macrophage colony stimulating factor 2 receptor, beta/CSF2RB	138981	U18373	22q12.2- q13.1
granulocyte-macrophage colony stimulating factor 2 receptor, alpha, Y chromosomal/CSF2RY	425000	*****	Yp11

Myeloid Differentiation	Granulocyte, Macrophage, Erythrocyte, and Platelet Differentiation	IL3 ligand/FMS-related tyrosine kinase 3 ligand/FLT3LG	600007	U03858	19q13.3
		STAT induced STAT inhibitor 3/SSI- 3	604176	NM_00395 5	*****
		erythropoietin/EPO	133170	NM_00079 9	7q21
		erythropoietin receptor/EPOR	133171	NM_00012 1	19p13.3- p13.2
		Janus kinase 2 (a protein tyrosine kinase)/JAK2	147796	NM_00497 2	9p24
		STAM-like protein containing SH3 and ITAM domains 2/STAM2	*****	NM_00584 3	*****
		ribosomal protein S7/RPS7	603474	NM_00101 1	19q13.2
		signal transducer and activator of transcription 5A/STAT5A	601511	NM_00315 2	17q11.2
		BCL-X/BCLX	600039	Z23115	*****
		thrombopoietin (MLV oncogene ligand, megakaryocyte growth and development factor)/THPO	600044	NM_00046 0	3q26.3-q27
		myeloproliferative leukemia virus oncogene/MPL/thrombopoietin receptor/TPOR	159530	NM_00537 3	1p34
		FMS-related tyrosine kinase 3/FLT3	136351	NM_00411 9	13q12

Table 4. Inflammation Gene List

Class	Pathway	Function	Name	OMIM	GID	Locus
-------	---------	----------	------	------	-----	-------

Major Histocompatibility Complex I	MHC class I HLA A/HLA-A	142800	AF148863	6p21.3
	MHC class I HLA B/HLA-B	142830	NM_005514	6p21.3
	MHC class I HLA C/HLA-C	142840	AF168611	6p21.3
	MHC class I HLA E/HLA-E	143010	NM_005516	6p21.3
	MHC class I HLA F/HLA-F	143110	X17093	6p21.3
	MHC class I HLA G/HLA-G	142871	AH005893	6p21.3
	beta-2-microglobulin/B2M	109700	NM_004048	15q21-q22
Major Histocompatibility Complex I- Related	thymocyte antigen CD1A/CD1A	188370	AF142665	1q21-q23
	thymocyte antigen CD1B/CD1B	188360	AF142666	1q21-q23
	thymocyte antigen CD1C/CD1C	188340	AF142667	1q21-q23
	thymocyte antigen CD1D/CD1D	188410	AF142668	1q21-q23
	thymocyte antigen CD1E/CD1E	188411	AF142669	1q21-q23
	interferon-gamma receptor 1/IFNGR1	107470	NM_000416	6q23-q24
MHC Class II Transcription	interferon-gamma receptor 2/IFNGR2	147569	NM_005534	21q22.1-q22.2
	TATA box binding protein (TBP)-associated factor, RNA polymerase II, A, 250kD/TAF2A	313650	NM_004606	Xq13
	interferon regulatory factor 1/IRF1	147575	NM_002198	5q31.1
	nuclear factor kappa-B DNA binding subunit 2/NFKB2	164012	NM_002502	10q24
	MHC class II HLA DR-alpha chain/HLA-DRA	142860	X83114	6p21.3

Major Histocompatibility Complex II	MHC class II HLA DR-beta chain/HLA-DRB	142857	M11161	6p21.3
	MHC class II HLA DP-alpha chain/HLA-DPA	142880	M23905	6p21.3
	MHC class II HLA DP-beta chain/HLA-DPB	142858	AH002893	6p21.3
	MHC class II HLA DM-alpha chain/HLA-DMA	142855	NM_006120	6p21.3
	MHC class II HLA DM-beta chain/HLA-DMB	142856	NM_002118	6p21.3
	MHC class II HLA DQ-alpha chain/HLA-DQA	146880	M11124	6p21.3
	MHC class II HLA DQ-beta chain/HLA-DQB	*****	M24364	6p21.3
	MHC class II HLA DN-alpha chain/HLA-DNA	142930	X02882	6p21.3
	MHC class II HLA DO-beta chain/HLA-DOB	600629	NM_002120	6p21.3
	MHC class II antigen gamma chain/CD74	142790	K01144	5q32
	antigen peptide transporter 1/MHC 1/TAP1	170260	NM_000593	6p21.3
	antigen peptide transporter 2/MHC 2/TAP2	170261	NM_000544	6p21.3
	interferon-gamma receptor 1/IFNGR1	107470	NM_000416	6q23-q24
	interferon-gamma receptor 2/IFNGR2	147569	NM_005534	21q22.1-q22.2
	regulatory factor X, 5 (influences HLA class II expression)/RFX5	601863	NM_000449	1q21.1-q21.3

Immune Discrimination (Self vs Non-Self)	Antigen Presentation and Recognition	MHC Class II Transcription	MHC class II transactivator/MHC2TA	600005	NM_000246	16p13		
			regulatory factor X-associated protein/RFXAP	601861	NM_000538	13q14		
		MHC Class II Transcription	regulatory factor X-associated ankyrin-containing protein/RFXANK	603200	NM_003721	19p12		
			regulatory factor X, 2 (influences HLA class II expression)/RFX2	142765	*****	19p13.3-p13.2		
			nuclear transcription factor, X-box binding 1/NFX1	603255	NM_002504	*****		
			nuclear transcription factor Y, alpha/NFYA	189903	NM_002505	6p21.3		
			nuclear transcription factor Y, beta/NFYB	189904	NM_006166	12q22-q23		
			T-cell antigen receptor, alpha subunit/TCRA	186880	Z24457	14q11.2		
		T-Cell Antigen Receptor Complex			T-cell antigen receptor, beta subunit/TCRB	186930	AF011643	7q35
					T-cell antigen receptor, gamma subunit/TCRG	186970	M17325	7p15-p14
					T-cell antigen receptor, delta subunit/TCRD	186810	L36384	14q11.2
					thymocyte antigen receptor complex CD3G, gamma polypeptide (TiT3 complex)/CD3G	186740	NM_000073	11q23
			thymocyte antigen receptor complex CD3D, delta polypeptide (TiT3 complex)/CD3D	186790	NM_000732	11q23		

Rearrangement of T-Cell Antigen Receptor Complex	thymocyte antigen receptor complex CD3E, epsilon polypeptide (TiT3 complex)/CD3E	186830	NM_000733	11q23
	thymocyte antigen receptor complex CD3Z, zeta polypeptide (TiT3 complex)/CD3Z	186780	NM_000734	1q22-q23
	(p50), sheep red blood cell receptor/CD2	186990	NM_001767	1p13.1
	ataxia telangiectasia mutated (includes complementation groups A, C and D)/ATM	208900	NM_000051	11q22.3
	recombination activating gene 1/RAG1	179615	NM_000448	11p13
	recombination activating gene 2/RAG2	179616	M94633	11p13
	interleukin 7 receptor/IL7R	146661	NM_002185	5p13
	v-myb avian myeloblastosis viral oncogene homolog/MYB	189990	NM_005375	6q22
	core binding factor, alpha 1 subunit/CBFA1	600211	AH005498	6p21
	core-binding factor, beta subunit/PEBP2B/CBFB	121360	L20298	16q22
	ligase I, DNA, ATP-dependent/LIG1	126391	NM_000234	19q13.2-q13.3
	ligase IV, DNA, ATP-dependent/LIG4	601837	NM_002312	13q22-q34
	X-ray repair, complementing defect in Chinese hamster/Ku antigen, 80 kD/KU80/XRCC5	194364	*****	2q35

	thyroid autoantigen, 70 kD/KU70/G22P1	152690	NM_001469	22q11-q13
Transcription of T-Cell Antigen Receptor Complex	GATA-binding protein 3/GATA3	131320	NM_002051	10p15
	long form transcription factor C-MAF/CMF	*****	AF055377	*****
	B-cell antigen CD25/interleukin 2 receptor, alpha chain/IL2RA/CD25	147730	10p15-p14	10p15-p14
	interleukin 2 receptor, beta/IL2RB	146710	NM_000878	22q11.2-q13
	interleukin 2 receptor, gamma chain/IL2RG	308380	NM_000206	Xq13
B-Cell Antigen Receptor Complex	transcription factor 1/hepatic nuclear factor /HNF1/albumin proximal factor/TCF1	142410	NM_000545	12q24.2
	lymphocyte antigen CD79A/immunoglobulin-associated alpha/CD79A	112205	NM_001783	19q13.2
	lymphocyte antigen CD79B/immunoglobulin-associated beta/CD79B	147245	L27587	17q23
	interferon regulatory factor 1/IRF1	147575	NM_002198	5q31.1
	interferon regulatory factor 2/IRF2	147576	NM_002199	4q35.1
	interferon consensus sequence binding protein 1/ICSBP1	601565	NM_002163	*****
	interferon alpha 1/IFNA1	147660	X02956	9p22
	interferon alpha 2/IFNA2	147562	Y11834	9p22

Interferons	Synthesis	interferon alpha 4/IFNA4	147564	*****	9p22
		interferon alpha 5/IFNA5	147565	NM_00216 ₉	9p22
		interferon alpha 6/IFNA6	147566	*****	9p22
		interferon alpha 7/IFNA7	147567	*****	9p22
		interferon alpha 8/IFNA8	147568	NM_00217 ₀	9p22
		interferon alpha 10/IFNA10	147577	NM_00217 ₁	9p22
		interferon alpha 13/IFNA13	147578	NM_00690 ₀	9p22
		interferon alpha 14/IFNA14	147579	NM_00217 ₂	9p22
		interferon alpha 16/IFNA16	147580	NM_00217 ₃	9p22
		interferon alpha 17/IFNA17	147583	*****	9p22
		interferon alpha 21/IFNA21	147584	NM_00217 ₅	9p22
		interferon beta 1/IFNB1	147640	NM_00217 ₆	9p21
		interferon beta 3/IFNB3	147860	K03196	Chr.8
		interferon gamma/IFNG	147570	L07633	12q14
		interferon omega 1/IFNW1	147553	NM_00217 ₇	9p21
	Receptors	interferon (alpha, beta and omega) receptor 1/IFNAR1	107450	X77722	21q22.1
		interferon (alpha, beta and omega) receptor 2/IFNAR2	602376	NM_00087 ₄	21q22.1
		interferon-gamma receptor 1/IFNGR1	107470	NM_00041 ₆	6q23-q24

interferon-gamma receptor 2/IFNGR2	147569	NM_005534	21q22.1-q22.2
interleukin enhancer binding factor 1/ILF1	147685	NM_004514	17q25
interleukin enhancer binding factor 2, 45 kD/ILF2	603181	NM_004515	*****
interleukin enhancer binding factor 3, 90 kD/ILF3	603182	NM_004516	*****
interleukin 1 alpha/IL1A2	147761	M15330	3q14
interleukin 1 beta/IL1B	147720	AF043335	2q14
apoptosis-related cysteine protease 1/interleukin 1-beta converting enzyme/ICE/caspase 1/CASP1	147678	NM_001223	11q22.2-q22.3
interleukin 2/IL2	147680	X01586	4q26-q27
interleukin 3/IL3	147740	NM_000588	5q31.1
interleukin 4/IL4	147780	NM_000589	5q31.1
interleukin 5/IL5	147850	NM_000879	5q31.1
interleukin 6/IL6	147620	AF048692	7p21
interleukin 7/IL7	146660	NM_000880	8q12-q13
interleukin 8/IL8	146930	M26383	4q12-q13
interleukin 9/IL9	146931	X17543	5q31.1
interleukin 10/IL10	124092	M57627	1q31-q32
interleukin 11 beta/IL11B	147681	NM_000881	19q13.3-q13.4

Synthesis

Interleukins	interleukin 12A (natural killer cell stimulatory factor 1, cytotoxic lymphocyte maturation factor 1, p35)/IL12A	161560	NM_002187	3p12-q13.2
	interleukin 12B/IL12B	161561	NM_000440	5q31.1-q33.1
	interleukin 13/IL13	147683	NM_002188	5q31
	interleukin 15/IL15	600554	U14407	4q31
	interleukin 16/IL16	603035	NM_004513	*****
	interleukin 17 (cytotoxic T-lymphocyte-associated serine esterase 3)/IL17	603149	NM_002190	2q31
	interleukin 18 (interferon-gamma-inducing factor)/IL18	600953	NM_001562	11q22.2-q22.3
	interleukin 1 receptor, type 1/IL1R1	147810	NM_000877	2q12
	interleukin 1 receptor, type 2/IL1R2	147811	NM_004633	2q12-q22
	interleukin 1 receptor-like 2/IL1RL2	*****	NM_003854	*****
	interleukin 1 receptor accessory protein/IL1RAP	602626	NM_002182	3q28
	B-cell antigen CD25/interleukin 2 receptor, alpha chain/IL2RA/CD25	147730	10p15-p14	10p15-p14
	interleukin 2 receptor, beta/IL2RB	146710	NM_000878	22q11.2-q13
	interleukin 2 receptor, gamma chain/IL2RG	308380	NM_000206	Xq13
	interleukin 3 alpha receptor/IL3RA	308385	M74782	Xp22.3

Receptors	interleukin 4 receptor precursor/IL4R	147781	NM_000418	16p12.1-p11.2
	interleukin 5 receptor alpha/IL5RA	147851	M96652	3p26-p24:
	interleukin 6 receptor/IL6R	147880	NM_000565	1q21
	interleukin 7 receptor/IL7R	146661	NM_002185	5p13
	interleukin 9 receptor/IL9R	300007	NM_002186	Xq28
	interleukin 10 receptor, alpha/IL10RA	146933	NM_001558	11q23.3
	interleukin 10 receptor beta/IL10RB	*****	NM_000628	*****
	interleukin receptor 11 alpha/IL11RA	600939	NM_004512	9p13
	interleukin 12 receptor, beta 1/IL12RB1	600939	NM_005535	9p13
	interleukin 12 receptor, beta 2/IL12RB2	601642	NM_001559	1p31.2
	interleukin 13 receptor, alpha 1/IL13RA1	300119	NM_001560	Chr.X
	interleukin receptor 13 alpha2/IL13A2	300130	X95302	Xq24
	interleukin 15 receptor, alpha/IL15RA	601070	NM_002189	10p15-p14
	interleukin 18 receptor 1/IL18R1	*****	NM_003855	*****
	interleukin 18 receptor accessory protein/IL18RAP	*****	NM_003853	*****
	LPS-Induced TNF-Alpha Factor/LITAF	603795	U77396	16p13.3-p12

Synthesis	tumor necrosis factor alpha/TNFA	191160	X01394	6p21.3
	tumor necrosis factor		NM_00059	
	beta/TNFB/lymphotoxin alpha/LTA	153440	5	6p21.3
	tumor necrosis factor		NM_00234	
	C/TNFC/lymphotoxin-beta/LTB	600978	1	6p21.3
	tumor necrosis factor ligand		NM_00332	
	superfamily, member 4/TNFSF4	603594	6	1q25
	tumor necrosis factor ligand		NM_00007	
	superfamily, member 5/TNFSF5	308230	4	Xq26
	tumor necrosis factor ligand		NM_00063	
	superfamily, member 6/TNFSF6	134638	9	1q23
	B-cell antigen CD70/tumor necrosis			
	factor ligand superfamily, member		NM_00125	
	7/TNFSF7/CD27 ligand/CD70	602840	2	19p13
	tumor necrosis factor ligand		NM_00124	
	superfamily, member 8/TNFSF8	603875	4	9q33
	tumor necrosis factor ligand		NM_00381	
	superfamily, member 10/TNFSF10	603598	0	3q26
	tumor necrosis factor ligand		NM_00370	
	superfamily, member 11/TNFSF11	602642	1	13q14
	tumor necrosis factor ligand		NM_00380	
	superfamily, member 12/TNFSF12	602695	9	17p13.3
	tumor necrosis factor ligand		NM_00657	
	superfamily, member 13B/TNFSF13B	603969	3	13q32-q34
	tumor necrosis factor ligand		*****	
	superfamily, member 15/TNFSF15	604052		9q33
	tumor necrosis factor receptor		NM_00106	
	superfamily, member 1A/TNFRSF1A	191190	5	12p13.2
	tumor necrosis factor receptor		NM_00106	
	superfamily, member 1B/TNFRSF1B	191191	6	1p36.3-p36.2

lymphotoxin beta receptor (TNFR superfamily, member 3/LTBR	600979	NM_00234 2	12p13
tumor necrosis factor receptor superfamily, member 4/TNFRSF4	600315	NM_00332 7	1p36
B-cell antigen CD40/tumor necrosis factor receptor superfamily, member 5/CD40/TNFRSF5	109535	NM_00125 0	20q12- q13.2
lymphocyte antigen CD95/tumor necrosis factor receptor superfamily, member 6/TNFRSF6/CD95	134637	NM_00004 3	10q24.1
tumor necrosis factor receptor superfamily, member 6B/TNFRSF6B	603361	NM_00382 3	20q13
T-cell antigen CD27/tumor necrosis factor receptor superfamily, member 7/CD27/TNFRSF7	186711	M63928	12p13
lymphocyte antigen CD30/tumor necrosis factor receptor superfamily, member 8/CD30/TNFRSF8	153243	NM_00124 3	1p36
tumor necrosis factor receptor superfamily, member 9/TNFRSF9	602250	NM_00156 1	1p36
tumor necrosis factor receptor superfamily, member	603611	NM_00384 4	8p21
tumor necrosis factor receptor superfamily, member	603612	NM_00384 2	8p22-p21
tumor necrosis factor receptor superfamily, member	603613	AF014794	8p22-p21
tumor necrosis factor receptor superfamily, member	603614	NM_00384 0	8p21
tumor necrosis factor receptor superfamily, member	603499	NM_00383 9	18q22.1

Receptors

**Tumor
Necrosis
Factor
Ligand
Superfamily**

Transforming Growth Factor	Synthesis	tumor necrosis factor receptor superfamily, member 11/TNFRSF11B	602643	NM_002546	8q24
		tumor necrosis factor receptor superfamily, member 12/TNFRSF12	603366	NM_003790	1p36.3
		tumor necrosis factor receptor superfamily, member 14/TNFRSF14	602746	NM_003820	1p36.3-p36.2
		tumor necrosis factor receptor superfamily, member 16/TNFRSF16	162010	NM_002507	17q21-q22
		tumor necrosis factor receptor superfamily, member 17/TNFRSF17	109545	Z14954	16p13.1
		tumor necrosis factor receptor superfamily, member 18/TNFRSF18	603905	*****	1p36.3
		transforming growth factor, transforming growth factor, beta-1/TGFB1	190170	NM_003236	2p13
		transforming growth factor, beta-2/TGFB2	190180	M60315	9q13.1-q13.2
		transforming growth factor, beta-3/TGFB3	190220	NM_003238	1q41
	Receptors	growth differentiation factor 1/GDF1	190230	NM_003239	14q24
		transforming growth factor, beta receptor I (activin A receptor type II-like kinase, 53kD)/TGFBRI	602880	NM_001492	19p12
		transforming growth factor, beta receptor II (70-80kD)/TGFBRII	190181	NM_004612	9q33-q34
		transforming growth factor, beta receptor III (betaglycan, 300kD)/TGFBRIII	190182	NM_003242	3p22
		transforming growth factor, beta receptor III (betaglycan, 300kD)/TGFBRIII	600742	NM_003243	1p33-p32

small inducible cytokine subfamily A (Cys-Cys), member 1/ inflammatory cytokine I309/SCYA1	182281	NM_00298 1	Chr.17
small inducible cytokine subfamily A (Cys-Cys), member 2/monocyte chemotactic protein 1/MCP1/SCYA2	158105	NM_00298 2	17q11.2- q12
small inducible cytokine subfamily A (Cys-Cys), member 3/macrophage inflammatory protein 1A/MIP1A/SCYA3	182283	NM_00298 3	17q11-q21
small inducible cytokine subfamily A (Cys-Cys), member 3-like 1/LD78- beta/SCYA3LI	601395	D90144	17q11.2
small inducible cytokine subfamily A (Cys-Cys), member 4/macrophage inflammatory protein 1B/MIP1B/SCYA4	182284	NM_00298 4	17q21-q23
small inducible cytokine subfamily A (Cys-Cys), member 4-like/macrophage inflammatory protein 1B/MIP1B/SCYA4L	603782	X52149	17q11.2
small inducible cytokine subfamily A (Cys-Cys), member 5/T-cell specific protein p228/TCP228/SCYA5	187011	NM_00298 5	17q11.2- q12
small inducible cytokine subfamily A (Cys-Cys), member 6/SCYA6	*****	*****	*****
small inducible cytokine subfamily A (Cys-Cys), member 7/monocyte chemotactic protein 3/MCP3/SCYA7	158106	AF043338	17q11.2- q12

small inducible cytokine subfamily A (Cys-Cys), member 8/monocyte chemotactic protein 2/MCP2/SCYA8	602283	NM_00562 3	17q11.2
small inducible cytokine subfamily A (Cys-Cys), member 9/10/SCYA9SCY10	*****	*****	*****
small inducible cytokine subfamily A (Cys-Cys), member 11/eotaxin/SCYA11	601156	NM_00298 6	17q21.1- q21.2
small inducible cytokine subfamily A (Cys-Cys), member 12/SCYA12	*****	*****	*****
small inducible cytokine subfamily A (Cys-Cys), member 13/monocyte chemotactic protein 4/MCP4/SCYA13	601391	NM_00540 8	17q11.2
small inducible cytokine subfamily A (Cys-Cys), member 14/new cc chemokine 2/NCC2/SCYA14	601392	NM_00459 0	17q11.2
small inducible cytokine subfamily A (Cys-Cys), member 15/leukotactin 1/LKN1/SCYA15	601393	NM_00416 7	17q11.2
small inducible cytokine subfamily A (Cys-Cys), member 16/new cc chemokine 4/NCC4/SCYA16	601394	NM_00459 0	17q11.2
small inducible cytokine subfamily A (Cys-Cys), member 17/thymus and activation-regulated chemokine/TARC/SCYA17	601520	NM_00298 7	16q13

small inducible cytokine subfamily A (Cys-Cys), member 18/pulmonary and activation-regulated chemokine/PARC/SCYA18	603757	NM_00298 8	17q11.2
small inducible cytokine subfamily A (Cys-Cys), member 19/macrophage inflammatory protein 3B/MIP3B/SCYA19	602227	NM_00627 4	9p13
small inducible cytokine subfamily A (Cys-Cys), member 20/macrophage inflammatory protein 3A/MIP3A/exodus 1/SCYA20	601960	NM_00459 1	2q33-q37
small inducible cytokine subfamily A (Cys-Cys), member 21/secondary lymphoid tissue chemokine/SLC/exodus 2/SCYA21	602737	NM_00298 9	9p13
small inducible cytokine subfamily A (Cys-Cys), member 22/SCYA22	602957	NM_00299 0	16q13
small inducible cytokine subfamily A (Cys-Cys), member 23/myeloid progenitor inhibitory factor 1/MPIF1/SCYA23	602494	NM_00506 4	*****
small inducible cytokine subfamily A (Cys-Cys), member 24/myeloid progenitor inhibitory factor 2/MPIF2/SCYA24	602495	NM_00299 1	7q11.23
small inducible cytokine subfamily A (Cys-Cys), member 25/thymus- expressed chemokine/TECK/SCYA25	602565	NM_00562 4	19p13.2

Synthesis
(see also
signaling and
transcription
factors
below)

**Cytokine-
Mediated
Immune
Regulation**

Chemokines	*****	AA716120	Chr. 7
small inducible cytokine subfamily A (Cys-Cys), member 26/eotaxin 3/SCYA26	*****	*****	Chr. 9
small inducible cytokine subfamily A (Cys-Cys), member 27/ALP/SCYA27	155730	NM_001511	4q12-q13
small inducible cytokine subfamily B (Cys-X-Cys), member 1/SCXB1	139110	NM_002089	4q12-q13
small inducible cytokine subfamily B (Cys-X-Cys), member 2/SCXB2	139111	AA935273	4q12-q13
small inducible cytokine subfamily B (Cys-X-Cys), member 3/SCXB3	173460	NM_002619	4q12-q13
small inducible cytokine subfamily B (Cys-X-Cys), member 4/SCXB4/platelet factor 4/PF4	600324	NM_002994	4q13-q21
small inducible cytokine subfamily B (Cys-X-Cys), member 5/epithelial- derived neutrophil-activating peptide 78/SCYB5	138965	U83303	4q12-q21
small inducible cytokine subfamily B (Cys-X-Cys), member 6/granulocyte chemotactic protein 2/GCP2/SCYB6	121010	NM_002704	4p12-q13
small inducible cytokine subfamily B (Cys-X-Cys), member 7/SCYB7	146930	M26383	4q12-q13
small inducible cytokine subfamily B (Cys-X-Cys), member 8/SCYB8/ interleukin 8/IL8	601704	AA037522	4q21
small inducible cytokine subfamily B (Cys-X-Cys), member 9/SCYB9			

small inducible cytokine subfamily B (Cys-X-Cys), member 10/SCYB10interferon (gamma)- induced protein of 10 kDa/INP10	147310	NM_00156 5	4q21
small inducible cytokine subfamily B (Cys-X-Cys), member 11/SCYB11	*****	AA361853	Chr. 4
small inducible cytokine subfamily B (Cys-X-Cys), member 12/SCYB12/stromal cell-driven factor/SDF1	600835	L36033	10q11.1
small inducible cytokine subfamily B (Cys-X-Cys), member 13/SCYB13	*****	*****	*****
small inducible cytokine subfamily B (Cys-X-Cys), member 14/SCYB14	604186	AC005738	5q31
small inducible cytokine subfamily C, member 1/lymphotactin/LTN/SCYC1	600250	NM_00299 5	1q21-q25
small inducible cytokine subfamily C, member 2/SCYC2	*****	NM_00317 5	*****
small inducible cytokine subfamily D (Cys-X3-Cys), member 1/fractalkine/neurotactin/NTT/NTN/S CYD1	601880	NM_00299 6	16q
chemokine (C-C motif) receptor 1/MIP1A receptor/CCR1	601159	NM_00129 5	3p21
chemokine (C-C motif) receptor 2/MCP1 receptor/CCR2	601267	NM_00064 7	3p21
chemokine (C-C motif) receptor 3/eotaxin receptor/CCR3	601268	NM_00183 7	3p21.3
chemokine (C-C motif) receptor 4/CCR4	*****	NM_00550 8	*****

chemokine (C-C motif) receptor 5/CCR5	601373	NM_000579	3p21
chemokine (C-C motif) receptor 6/G protein-coupled receptor 29/GPR29/CCR6	601835	NM_004367	6q27
chemokine (C-C motif) receptor 7/epstein-barr virus induced gene 1/EBI1/CCR7	600242	NM_001838	17q12- q21.2
chemokine (C-C motif) receptor 8/CCR8	601834	NM_005201	3p22
chemokine (C-C motif) receptor 9/chemokine-binding protein 2/CCBP2/CCR9	602648	NM_006641	3p21.3
chemokine (C-C motif) receptor 10/CCR10	*****	U94888	*****
chemokine (C-X-C motif), receptor 3/G protein-coupled receptor 9/GPR9/CXCR3	600894	NM_001504	8p12-p11.2
chemokine (C-X-C motif), receptor 4/fusin/CXCR4	162643	NM_003467	2q21
chemokine (C-X3-C motif), receptor 1/fractalkine receptor/CX3CR1	601470	NM_001337	3pter-p21
interleukin 8 receptor, alpha/IL8RA	146929	NM_000634	2q35
interleukin 8 receptor beta/IL8RB	146928	NM_001557	2q35
chemokine (C motif) XC receptor 1/G protein-coupled receptor 5/GPR5/CCXCR1	600552	NM_005283	3p21.3- p21.1

**C-Motif
Chemokine
Receptors**

Synthesis	macrophage migration-inhibitory factor (glycosylation-inhibiting factor) GM-6000	153620	NM_002415	22q11.2
	leukemia inhibitory factor/LIF	159540	NM_002309	22q12.1-q12.2
	oncostatin M	165095	AF129855	22q12.1-q12.2
	ciliary neurotrophic factor/CNTF	118945	NM_000614	11q12.2
	epidermal growth factor/EGF	131530	NM_001963	4q25
	pre-B cell stimulating factor homologue/SDF1A	600835	L36034	10q11.1
	cardiotrophin 1	600435	*****	*****
	mast cell growth factor/MGF	184745	NM_003994	12q22
	granulocyte-macrophage colony stimulating factor 2/CSF2	138960	NM_000758	5q31.1
	macrophage-specific colony-stimulating factor/CSF1	120420	AH005300	1p21-p13
	granulocyte colony stimulating factor 3/CSF3	138970	NM_000759	17q11.2-q12
	epidermal growth factor receptor EGFR	131550	NM_005228	7p12.3-p12.1
	ciliary neurotrophic factor receptor/CNTFR	118946	NM_001842	9p13
	oncostatin M receptor/OSMR	601743	NM_003999	*****
	neutrophil chemotactic response receptor/gpl30	162820	*****	7q22-qter
Other Growth Factors				

Receptors	colony stimulating factor 1 receptor/CSFR1	164770	U63963	5q33.2-q33.3
	granulocyte-macrophage colony stimulating factor 2 receptor, alpha, low-affinity/CSF2RA	306250	NM_006140	Xp22.32
	granulocyte-macrophage colony stimulating factor 2 receptor, beta/CSF2RB	138981	U18373	22q12.2-q13.1
	granulocyte-macrophage colony stimulating factor 2 receptor, alpha, Y chromosomal/CSF2RY	425000	*****	Yp11
	myelocyte antigen CD105/endoglin/ENG/TGFB receptor component/CD105	131195	NM_000118	9q34.1
	leukocyte antigen CD 97/CD97	601211	NM_001784	19p13.2-p13.12
	signal transducer and activator of transcription 1/STAT 1	600555	*****	2q32.2-q32.3
	signal transducer and activator of transcription 2, 113kD/STAT2	600556	NM_005419	*****
	signal transducer and activator of transcription 3/STAT3	102582	NM_003150	17q21
	signal transducer and activator of transcription 6, interleukin-4 induced/STAT6	601512	NM_003153	12q13
	signal transducing adaptor molecule (SH3 domain and ITAM motif) 1/STAM	601899	NM_003473	10p14-p13
	STAM-like protein containing SH3 and ITAM domains 2/STAM2	*****	NM_005843	*****

interferon-stimulated transcription factor 3, gamma (48kD)/ISGF3G	147574	NM_006084	14q11.2
interferon, alpha-inducible protein 27/IFI27	600009	NM_005532	14q32
interferon, alpha-inducible protein (clone IFI-6-16)/GIP3	147572	NM_002038	1p35
Janus kinase 1 (protein tyrosine kinase)/JAK1	147795	NM_002227	1p31.3
Janus kinase 3 (protein tyrosine kinase)/JAK3	600173	NM_000215	19p13.1
interleukin-1 receptor-associated kinase M/IRAK-M	*****	NM_007199	*****
interleukin-1 receptor-associated kinase 1/IRAK1	601108	NM_001569	Xq28
interleukin-1 receptor-associated kinase 1/IRAK2	603304	NM_001570	*****
nuclear factor, interleukin 3 regulated/NFIL3	*****	NM_005384	*****
nuclear factor of activated T-cells, cytoplasmic 1/NFATC1	600489	NM_006162	18q23
nuclear factor of activated T-cells, cytoplasmic 2/NFATC2	600490	*****	20q13.2-q13.3
nuclear factor of activated T-cells, cytoplasmic 3/NFATC3	602698	L41066	16q13-q24
nuclear factor of activated T-cells, cytoplasmic 4/NFATC4	602699	L41067	*****
caspase 1, apoptosis-related cysteine protease (interleukin 1, beta, convertase)/CASPI	147678	NM_001223	11q22.2-q22.3

TGFB inducible early growth response/TIEG	601878	NM_005655	*****
TGFB inducible early growth response 2/TIEG2	603301	NM_003597	*****
eukaryotic translation initiation factor 3, subunit 8 (110kD)/EIF3S8	603911	NM_003752	1p34.1
MAD (mothers against decapentaplegic) homolog 1/MADH1	601595	NM_005900	4q28
homolog of Xenopus forkhead activin signal transducer-1 /FAST1	603621	NM_003923	8q24.3
interleukin 1 receptor accessory protein/IL1RAP	602626	NM_002182	3q28
CCAAT/enhancer binding protein (C/EBP), delta/CEBPD	189965	NM_005195	20q13.1
T-lymphocytes-specific interleukin 2 inhibitor/transcription factor 8/TCF8/	189909	U12170	10p11.2
cAMP responsive element binding protein 1/CREB1	123810	NM_004379	2q32.3-q34
interferon-stimulated transcription factor 3, gamma (48kD)/ISGF3G	147574	NM_006084	14q11.2
interferon regulatory factor 3/IRF3	603734	NM_001571	19q13.3-q13.4
lymphocyte specific interferon regulatory factor/LSIRF/interferon regulatory factor 4/IRF4	601900	U52683	6p25-p23
TNF receptor-associated factor 1/TRAF1	601711	NM_005658	9q33-q34
TNF receptor-associated factor 2/TRAF2	601895	U12597	9q34

Cytokine Response	Signaling and Transcription Factors	TNF receptor-associated factor 3/TRAF3	601896	NM_00330 0	*****
		TNF receptor-associated factor 4/TRAF4	602464	NM_00429 5	17q11-q12
		TNF receptor-associated factor 5/TRAF5	602356	AB000509	1q32
		TNF receptor-associated factor 6/TRAF6	602355	NM_00462 0	*****
		TRAF family member-associated NFKB activator/TANK	603893	NM_00418 0	2q24-q31
		mitogen activated protein kinase PRKM1/MAPK1	176948	NM_00274 5	22q11.2
		mitogen activated protein kinase PRKM3/MAPK3	601795	X60188	16p11.2
		mitogen activated protein kinase PRKM4/MAPK4	176949	NM_00274 7	18q12-q21
		mitogen activated protein kinase PRKM6/MAPK6	602904	NM_00274 8	*****
		mitogen activated protein kinase PRKM7/MAPK7	602521	NM_00274 9	17p11.2
		mitogen activated protein kinase JNK1/PRKM8/MAPK8	601158	L26318	*****
		mitogen activated protein kinase JNK2/PRKM9/MAPK9	602896	U09759	5q35
		mitogen activated protein kinase JNK3/PRKM10/MAPK10	602897	U35003	*****
		mitogen activated protein kinase PRKM11/MAPK11	602898	AF031135	*****
		mitogen activated protein kinase SAPK3/MAPK12	602399	NM_00296 9	22q13.3

mitogen activated protein kinase PRKM13/MAPK13	602899	NM_00275 4	*****
mitogen activated protein kinase SAPK2A/MAPK14	600289	NM_00131 5	6p21.3- p21.2
mitogen-activated protein kinase kinase 1/MAP2K1	176872	NM_00275 5	15q22.1- q22.33
mitogen-activated protein kinase kinase 2/MAP2K2	601263	L11285	*****
mitogen-activated protein kinase kinase 3/MAP2K3	602315	NM_00275 6	17q11.2
mitogen-activated protein kinase kinase 4/MAP2K4	601335	NM_00301 0	17p11.2
mitogen-activated protein kinase kinase 5/MAP2K5	602520	NM_00275 7	*****
mitogen-activated protein kinase kinase 6/MAP2K6	601254	U39065	*****
mitogen-activated protein kinase kinase 7/MAP2K7	603014	NM_00504 3	*****
protein kinase C alpha/PRKCA	176960	NM_00273 7	17q22- q23.2
protein kinase C beta/PRKCB	176970	X06318	16p11.2
protein kinase C, delta/PRKCD	176977	NM_00625 4	3p
protein kinase C gamma/PRKCG	176980	*****	19q13.4
protein kinase C, theta/PRKCT	600448	NM_00625 7	10p15
protein kinase C, zeta/PRKCZ	176982	NM_00274 4	*****
casein kinase 1 alpha 1	600505	NM_00189 2	13q13

casein kinase 1 gamma 2	602214	U89896	19p13.3
casein kinase 1 delta	600864	NM_00189 3	17q25
casein kinase 1 epsilon	600863	NM_00189 4	22q12-q13
casein kinase 2 alpha 1	115440	J02853	20p13
casein kinase 2 alpha 2	115442	NM_00189 6	16p13.3- p13.2
casein kinase 2 beta	115441	X57152	6p21.3
phosphatidylinositol 3-kinase, regulatory subunit, polypeptide 1 (p85, alpha)/PIK3R1	171833	M61906	5q13
phosphatidylinositol 3-kinase, regulatory subunit, polypeptide 2 (p85, beta)/PIK3R2	603157	NM_00502 7	19q13.2- q13.4
phosphatidylinositol 3-kinase, regulatory subunit, polypeptide 3 (p55, gamma)/PIK3R3	*****	NM_00362 9	*****
phosphoinositide-3-kinase, catalytic, alpha polypeptide/PIK3CA	171834	NM_00621 8	3q26.3
phosphoinositide-3-kinase, catalytic, beta polypeptide/PIK3CB	602925	NM_00621 9	*****
phosphatidylinositol 3-kinase, catalytic, delta polypeptide/PIK3CD	602839	NM_00502 6	1p36.2
phosphatidylinositol 3-kinase, catalytic, gamma polypeptide/PIK3CG	601232	NM_00264 9	*****
peptidyl-prolyl isomerase A/cyclophilin A/PPIA	123840	Y00052	7p13
peptidyl-prolyl isomerase B/cyclophilin B/PPIB	123841	M60857	chr. 15

Biosynthesis	peptidyl-prolyl isomerase C/cyclophilin C/PPIC	123842	S71018	*****
	peptidyl-prolyl isomerase D/cyclophilin D/PPID	601753	NM_005038	4q31.3
	peptidyl-prolyl isomerase E/cyclophilin E/PPIE	*****	NM_006112	*****
	peptidyl-prolyl isomerase-like/PPIL1	601301	AF090992	6p21.1
	FK506 binding protein			
Cyclophilins	1A/immunophilin/FKBP1A	186945	NM_000801	20p13
	FK506 binding protein			
	2/immunophilin/FKBP2	186946	NM_004470	1q13.1-q13.3
	FK506 binding protein			
	4/immunophilin/FKBP4	600611	NM_002014	*****
	FK506 binding protein			
	5/immunophilin/FKBP5	602623	NM_004117	*****
	calcium modulating cyclophilin ligand/CALMLG	601118	NM_001745	5q23
Response	protein phosphatase 3, catalytic subunit, alpha isoform/calcineurin	114105	M29550	4q21-q24
	protein phosphatase 3, catalytic subunit, beta isoform/calcineurin	114106	M30773	10q21-q22
	protein phosphatase 3, catalytic subunit, gamma isoform/calcineurin	114107	NM_005605	Chr.8
	protein phosphatase 3, regulatory subunit B, alpha isoform/calcineurin	601302	*****	2p16-p15
	calmodulin 1/CALM1	114180	AH005370	14q24-q31
	calmodulin 2/CALM2	114182	NM_001743	2p21.3-p21.1
	calmodulin 3/CALM3	114183	NM_005184	9q13.2-q13.3

Non-Cytokine Mediated Immune Regulation	Biosynthesis	cytochrome P450, subfamily XXI (steroid 21-hydroxylase)/CYP21	201910	M13936	6p21.3
		cytochrome P450, subfamily XIB (steroid 18-beta-hydroxylase), polypeptide 2/CYP11B2	124080	NM_000498	8q21
		cytochrome P450, subfamily XIB (steroid 11-beta-hydroxylase), polypeptide 1/CYP11B1	202010	NM_000497	8q21
Corticosteroids	Receptors and Signaling	nuclear receptor subfamily 3, group C, member 1/NR3C1	138040	NM_000176	5q31
		melanocortin 2 receptor/ACTH receptor/MC2R	202200	NM_000529	18p11.2
		mineralocorticoid receptor/MCR/nuclear receptor subfamily 3, group C, member	600983	NM_000901	4q31.1
		heat shock 70kD protein 1/HSPA1A	140550	NM_005345	6p21.3
		heat shock 70kD protein-like 1/HSPA1L	140559	NM_005527	6p21.3
		heat shock 70kD protein 1/HSPA1B	603012	NM_005346	6p21.3
		heat shock 90-kD protein 1, alpha subunit/HSPCA	140571	*****	1q21.2-q22
		heat shock 90-kD protein 1, beta subunit/HSPCB	140572	J04988	6p12
		FK506-binding protein 4 (59kD)/FKBP4	600611	NM_002014	*****
		corticosteroid binding globulin precursor/CBG	122500	NM_001756	14q32.1
		hydroxy-D-5-steroid dehydrogenase, 3b- and steroid D-isomerase 2/HSD3B2	201810	NM_000198	1p13.1

Metabolism	UDP glycosyltransferase 1/UGT1	191740	NM_001072	Chr. 12
	UDP glycosyltransferase family 2, member B4/UGT2B4	600067	NM_001073	4q13
	UDP glycosyltransferase family 2, member B7/UGT2B7	600068	NM_001074	1q14
	UDP glycosyltransferase 2 family, polypeptide B11/UGT2B11	603064	NM_001073	*****
	UDP glycosyltransferase family 2, member B15/UGT2B15	600069	NM_001076	4q13
	UDP glycosyltransferase family 2, member B17/UGT2B17	601903	NM_001077	1q14
	Dehydroepiandrosterone (DHEA)-preferring sulfotransferase, family 2A, member 1/SULT2A1	125263	NM_003167	19q13.3
	estrogen-preferring	600043	NM_005420	4q13.1
	vitamin D (1,25- dihydroxyvitamin D3) receptor/VDR	601769	NM_000376	12q12-q14
	Retinoic acid receptor, alpha/RARA	180240	NM_0000964	17q12
Retinoic Acid	Retinoic acid receptor, beta/RARB	180220	NM_0000965	3p24
	Retinoic acid receptor, gamma/RARG	180190	M57707	12q13
	T-cell antigen CD4/LEU3/CD4	186940	X87579	12pter-p12
	T-cell antigen CD6/T-cell differentiation antigen/CD6	186720	NM_006725	Chr.11
	lymphocyte antigen CD5/LEU1/CD5	153340	X04391	11q13
	thymocyte antigen CD7/Tp41/CD7	186820	NM_006137	17q25.2-q25.3

T-Cell	lymphocyte antigen CD19/B-lymphocyte antigen/CD19	107265	X13312	16p11.2
	B-lymphocyte antigen CD80 (CD28 antigen ligand 1, B7-1 antigen)/CD80	112203	NM_005191	3q21
	CD86 antigen (CD28 antigen ligand 2, B7-2 antigen)/CD86	601020	NM_006889	3q21
	T-cell antigen CD28 (Tp44)/CD28	186760	NM_006139	2q33-q34
	T-cell antigen receptor, beta subunit/TCRB	186930	AF011643	7q35
	CD3G antigen, gamma polypeptide (TiT3 complex)/CD3G	186740	NM_000073	11q23
	CD3D antigen, delta polypeptide (TiT3 complex)/CD3D	186790	NM_000073	11q23
	CD3E antigen, epsilon polypeptide (TiT3 complex)/CD3E	186830	NM_000073	11q23
	CD3Z antigen, zeta polypeptide (TiT3 complex)/CD3Z	186780	NM_000073	1q22-q23
	leukocyte common antigen	151460	M23492	1q31-q32
	T-cell antigen CD69/p60/CD69	107273	NM_001781	12p13-p12
	lymphoblast antigen CD38/ADP-ribose cyclase/cyclic ADP-ribose hydrolase/CD38	107270	NM_001775	4p15
	lymphoblast antigen CD39/vascular ATP diphosphohydrolase/CD39	601752	NM_001776	10q24
	lymphocyte antigen CD73/5' nucleotidase/NT5/ CD73	129190	NM_002526	6q14-q21
	Receptors			

**Activation,
Differentiation,
and
Proliferation**
(excluding
genes from
cytokine
section
above)

leukocyte antigen CD23/low-affinity receptor II for Fc portion of IgE/FCER2/CD23	151445	NM_00200 2	19p13.3
macrophage antigen CD 64/high- affinity receptor IA for Fc fragment of IgG/FCGR1A	146760	Y10206	1q21.2- q21.3
lymphocyte antigen CD57/LEU7/CD57	151290	*****	Chr.11
lymphocyte function-associated antigen, type 3/LAF3/LEU7/CD58	153420	NM_00177 9	1p13
lymphocyte antigen CD45/protein tyrosine phosphatase, receptor type, c polypeptide/PTPRC/CD45	151460	NM_00283 8	1q31-q32
T-cell antigen receptor, gamma subunit/TCRG	186970	M17325	7p15-p14
T-cell antigen receptor, delta subunit/TCRD	186810	L36384	14q11.2
T-cell antigen CD8, alpha polypeptide (p32)/CD8A	186910	NM_00176 8	2p12
T-cell antigen CD8, beta polypeptide/CD8B	186730	AH003859	2p12
T-cell antigen CD28 (Tp44)/CD28	186760	NM_00613 9	2q33-q34
cytotoxic T-lymphocyte-associated 4/CTLA4	123890	L15006	2q33
T-cell antigen receptor, alpha subunit/TCRA	186880	Z24457	14q11.2
CD89 antigen/receptor for Fc fragment of IgA/FCAR/CD89	147045	NM_00200 0	19q13.4
T-cell activation antigen p250/TP250	186710	*****	11pter- p11.2

Signaling	signaling lymphocytic activation molecule/SLAM	603492	NM_003037	*****
	T cell receptor-associated protein tyrosine kinase ZAP-70/ZAP70	176947	S69911	2q12
	v-mos Moloney murine sarcoma viral oncogene homolog/MOS	190060	NM_005372	8q11
	IL2-inducible T-cell kinase/ITK/T-cell tyrosine kinase EMT/EMT	186973	NM_005546	5q32
	mature T-cell proliferation 1/MTCPI	300116	Z24459	Xq28
	lymphocyte-specific protein tyrosine kinase/LCK	153390	NM_005356	1p35-p34.3
	B-cell antigen CD20/B-lymphocyte differentiation antigen B1/CD20	112210	AH003353	11q13
	B-cell antigen CD72/CD72	107272	NM_001782	9p
	macrophage protein 1/NRAMP1/solute carrier family 11, member 1/SLC11A2	600266	AH002806	2q35
	macrophage protein 2/NRAMP2/solute carrier family 11, member 2/SLC11A2	600523	AB015355	12q13
B-Cell Activation, Differentiation, and Proliferation (excluding genes from cytokine)	T-lymphocyte antigen CDW52 (CAMPATH-1 antigen)/CDW52	114280	NM_001803	*****
	B-cell antigen CD22/CD22	107266	NM_001771	19q13.1
	B-cell antigen CD24/CD24	600074	X69397	6q21
	B-cell antigen CD40/tumor necrosis factor receptor superfamily, member 5/CD40/TNFRSF5	109535	NM_001250	20q12-q13.2
Receptors				

section above)	leukocyte antigen CD156/disintegrin and metalloprotease domain 8/ADAM8/CD156	602267	NM_00110 9	10q26.3
	platelet antigen CD151/platelet- endothelial cell tetraspan antigen 3/PETA3/CD151	602243	NM_00435 7	11p15.5
	IIA for Fc fragment of IgG/FCGR2A/CD32	146790	NM_00400 1	1q21-q23
	activated leucocyte cell adhesion molecule/CD6 ligand/ALCAM	601662	NM_00162 7	3q13.1- q13.2
	regulator of G-protein signaling 1/RGS1	600323	NM_00292 2	1q31
Growth Factors	macrophage-specific colony- stimulating factor/CSF1	120420	AH005300	1p21-p13
	granulocyte-macrophage colony stimulating factor 2/CSF2	138960	NM_00075 8	5q31.1
	granulocyte colony stimulating factor 3/CSF3	138970	NM_00075 9	17q11.2- q12
	colony stimulating factor 1 receptor/CSFR1	164770	U63963	5q33.2- q33.3
Myeloid Progenitor Cell Differentiation on and Proliferation (excluding genes from cytokine	granulocyte-macrophage colony stimulating factor 2 receptor, alpha, Y chromosomal/CSF2RY	425000	*****	Yp11
	granulocyte-macrophage colony stimulating factor 2 receptor, alpha, low-affinity/CSF2RA	306250	NM_00614 0	Xp22.32
	granulocyte-macrophage colony stimulating factor 2 receptor, beta/CSF2RB	138981	U18373	22q12.2- q13.1

section above)	Signaling	CCAAT/enhancer binding protein (C/EBP), beta/CEBPB	189965	NM_00519 4	20q13.1
		CCAAT/enhancer binding protein (C/EBP), epsilon/CEBPE	600749	NM_00180 5	14q11.2
		flt3 ligand/FMS-related tyrosine kinase 3 ligand/FLT3LG	600007	U03858	19q13.3
		FMS-related tyrosine kinase 3/FLT3	136351	NM_00411 9	13q12
		myeloid differentiation primary response gene (88)/MYD88	602170	NM_00246 8	3p22-p21.3
		BCL2	151430	M13994	18q21.3
		BCL-X/BCLX	600039	Z23115	*****
		BCL2 associated protein/BAX	600040	L22473	19q13.3- q13.4
		BCL2-antagonist/killer 1/BAK1	600516	NM_00118 8	6p21.3- p21.2
		BCL2-associated athanogene 1/BAG1	601497	NM_00432 3	9p12
		BCL2-associated athanogene 2/BAG2	603882	NM_00428 2	*****
		BCL2-associated athanogene 3/BAG3	603883	AF095193	*****
		BCL2-associated athanogene 4/BAG4	603884	AF095194	*****
		BCL2-associated athanogene 5/BAG5	603885	AF095195	*****
		BCL-X/BCL-2 binding protein/BAD	603167	AF021792	*****
		BCL2-like 1/BCL2L1	600039	NM_00119 1	*****
		BCL2-like 2/BCL2L2	601931	NM_00405 0	14q11.2- q12
		BCL2-like 11 (apoptosis facilitator)/BCL2L11	603827	NM_00653 8	*****

BCL2-related protein A1/BCL2A1	601056	Y09397	15q24.3
BCL2-interacting protein harikari/HRK	603447	NM_00380 6	*****
Bcl-2 interacting killer/BIK	603392	U34584	*****
tumor protein p53/TP53	191170	X02469	17p13.1
superfamily, member 6/FAS/TNFRSF6	134637	NM_00004 3	10q24.1
nuclear factor kappa-B DNA binding subunit 1/NFKB1	164011	M58603	4q23-q24
nuclear factor kappa-B DNA binding subunit 2/NFKB2	164012	NM_00250 2	10q24
apoptosis-related cysteine protease 1/caspase 1/CASP1	147678	L27475	11q22.2- q22.3
apoptosis-related cysteine protease 1/caspase 1/CASP2	600639	*****	7q35
apoptosis-related cysteine protease 1/caspase 1/CASP3	600636	NM_00434 6	4q35, 4q33 q35.1
apoptosis-related cysteine protease 1/caspase 1/CASP4	602664	NM_00434 7	11q22.2- q22.3
apoptosis-related cysteine protease 1/caspase 1/CASP5	602665	NM_00434 7	11q22.2- q22.3
apoptosis-related cysteine protease 1/caspase 1/CASP6	601532	NM_00122 6	4q25-q25
apoptosis-related cysteine protease 1/caspase 1/CASP7	601761	NM_00122 7	10q25.1- q25.2
apoptosis-related cysteine protease 1/caspase 1/CASP8	601763	NM_00122 8	2q33-q34
apoptosis-related cysteine protease 1/caspase 1/CASP9	602234	*****	*****

Apoptosis

Apoptosis
(additional
genes in
Oncology)

**Cell-
Mediated
Inflammation**

apoptosis-related cysteine protease 1/caspase 1/CASP10	601762	NM_001230	2q33-q34
apoptosis-related cysteine protease 1/caspase 1/CASP13	603653	NM_003723	*****
ADP-ribosyltransferase (NAD ⁺ ; poly (ADP-ribose) polymerase)/PARP/ADPRT	173870	NM_001618	1q42
poly (ADP-ribose) glycohydrolase/PARG	603501	NM_003631	10q11.23
lymphocyte antigen CD11A/integrin, alpha-L/CD11A/ITGAL	153370	NM_002209	16p11.2
lymphocyte antigen CD11B/integrin, alpha-M/CD11B/ITGAM	120980	NM_000632	16p11.2
lymphocyte antigen CD11C/integrin, alpha-X/CD11C/ITGAX	151510	NM_000887	16p11.2
lymphocyte antigen CD11D/integrin, alpha-D/CD11D/ITGAD	602453	NM_005353	16p11.2
antigen CD51/integrin, alpha- V/vitronectin receptor/CD51/ITGAV	193210	NM_002210	2q31-q32
integrin, alpha 1/ITGA1	192968	*****	Chr.5
integrin, alpha 2/ITGA2	192974	NM_002203	5q23-q31
integrin, alpha 3/ITGA3	*****	NM_005501	*****
integrin, alpha 4/ITGA4	192975	NM_000885	2q31-q32
integrin, alpha5/fibronectin receptor, alpha subunit/FNRA/ITGA5	135620	NM_002205	12q11-q13
integrin, alpha 6/ITGA6	147556	NM_000210	Chr.2

Integrins	integrin, alpha 7/ITGA7	600536	NM_002206	12q13
	integrin, alpha 8/ITGA8	604063	L36531	*****
	integrin, alpha 9/ITGA9	603963	L24158	3p21.3
	integrin, alpha 10/ITGA10	604042	NM_003637	*****
	antigen CD29/integrin, beta-1/CD29/ITGB1	135630	NM_002211	10p11.2
	leukocyte antigen CD18/integrin beta chain, beta 2/CD18/ITGB2	600065	NM_000211	21q22.3
	platelet antigen CD61/integrin, beta-3/CD61/ITGB3	173470	NM_000212	17q21.32
	integrin, beta 5/ITGB5	147561	NM_002213	*****
	integrin, beta 6/ITGB6	147558	NM_000888	Chr.2
	integrin, beta 7/ITGB7	147559	NM_000889	12q13.13
	integrin, beta-like 1 (with EGF-like repeat domains)/ITGBL1	604234	NM_004791	13q33
	erythrocyte antigen CD47/Rh-related antigen, integrin-associated signal transducer/CD47	601028	NM_001777	3q13.1-q13.2
	integrin-linked kinase/ILK	602366	NM_004517	11p15.5-p15.4
	selectin E/endothelial adhesion molecule 1/ELAM1/SELE	131210	NM_000450	1q23-q25
Selectins	granulocyte antigen CD62/platelet alpha-granule membrane protein/selectin P/CD62/SELP	173610	NM_003005	1q23-q25

Adhesion and Migration	selectin L/lymphocyte adhesion molecule 1/LAM1/SELL	153240	NM_000655	1q23-q25
	T-cell antigen CD8, alpha polypeptide (p32)/LEU2/CD8A	186910	NM_001768	2p12
	T-cell antigen CD8, beta polypeptide/CD8B	186730	AH003859	2p12
	leukocyte antigen CD9/MIC3/CD9	143030	NM_001769	12p13
	activated leucocyte cell adhesion molecule/CD6 ligand/ALCAM	601662	NM_001627	3q13.1-q13.2
	mucosal addressin cell adhesion molecule-1/MACAM1	102670	NM_007164	19p13.3
	platelet antigen CD151/platelet-endothelial cell tetraspan antigen 3/PETA3/CD151	602243	NM_004357	11p15.5
	CD36/thrombospondin receptor/platelet collagen	173510	NM_000072	7q11.2
	leukocyte antigen CD37/CD37	151523	NM_001774	19p13-q13.4
	platelet antigen CD31/platelet-endothelial cell adhesion molecule 1/PECAM1/CD31	173445	NM_000442	17q23
	T-cell antigen CD26/dipeptidylpeptidase IV/CD26	102720	NM_001935	2q23
	lymphocyte antigen CD44/hermes antigen/CD44	107269	AF098641	11pter-p13
	B-cell antigen CD 48/B-cell activation marker/BCM1/BLAST1	109530	NM_001778	1q21.3-q22
	leukocyte antigen CD53/tetraspan antigen/CD53	151525	AJ243474	1p21-p13.3

**Other
Adhesion
Molecules**

B-cell antigen CD54/intercellular adhesion molecule 1/ICAM1/CD54	147840	NM_000201	19p13.3-p13.2
intercellular adhesion molecule 2/ICAM2	146630	NM_000873	17q23-q25
intercellular adhesion molecule 3/ICAM3	146631	NM_002162	19p13.3-p13.2
myeloid antigen CD33/p67/CD33	159590	NM_001772	19q13.3-q13.4
granulocyte antigen CD66/biliary glycoprotein/CD66	109770	NM_001712	19q13.2
leukocyte antigen CD81/target of antiproliferative antibody 1/TAPAI/CD81	186845	NM_004356	11p
leukocyte antigen CD82/R2/suppression of tumorigenicity 1/STES1/CD82	600623	NM_002231	11p11.2
killer cell lectin-like receptor subfamily B, member 1/KLRB1	602890	NM_002258	12p13-p12
killer cell lectin-like receptor subfamily C, member 1/KLRC1	161555	NM_002259	12p13.2-p12.3
killer cell lectin-like receptor subfamily C, member 2/KLRC2	602891	NM_002260	12p13.2-p12.3
killer cell lectin-like receptor subfamily C, member 3/KLRC3	602892	NM_002261	12p13.2-p12.3
killer cell lectin-like receptor subfamily C, member 4/KLRC4	602893	NM_003497	12p13.2-p12.3
killer cell antigen CD94/killer cell lectin-like receptor subfamily D, member 1/KLRD1/CD94	602894	NM_002262	12p13.2-p12.3
T-cell antigen CD99/MIC2/CD99	313470	NM_002414	Xpter-p22.32

	leukocyte antigen CD100/semaphorin 4D/SEMA4D/CD100	601866	NM_006378	9q22-q31
	hematopoietic progenitor cell antigen CD34/CD34	142230	AH000040	1q32
	macrophage antigen CD68/macrosialin/CD68	153634	NM_001251	17p13
	cadherin 2, N-cadherin (neuronal)/CDH2	114020	NM_001792	18q11.2
	receptor for advanced glycation end products/RAGE	600214	AJ133822	6p21.3
	leukocyte antigen CD43/sialophorin/SPN/CD43	182160	NM_003123	16p11.2
	vascular cell adhesion molecule 1/VCAM1	192225	NM_001078	1p32-p31
	UDP-Gal:betaGlcNAc beta 1,4-galactosyltransferase, polypeptide 1/B4GALT1	137060	NM_001497	9p13
	UDP-Gal:betaGlcNAc beta 1,4-galactosyltransferase, polypeptide 2/B4GALT2	604013	NM_003780	1p33-p32
	UDP-Gal:betaGlcNAc beta 1,4-galactosyltransferase, polypeptide 3/B4GALT3	604014	NM_003779	1q23
	UDP-Gal:betaGlcNAc beta 1,4-galactosyltransferase, polypeptide 4/B4GALT4	604015	AF038662	3q13.3
	UDP-Gal:betaGlcNAc beta 1,4-galactosyltransferase, polypeptide 5/B4GALT5	604016	NM_004776	Chr.11
Glycosyltransferases	Glycosyltransferases			

UDP-Gal:betaGlcNAc beta 1,4-galactosyltransferase, polypeptide 6/B4GALT6	604017	AF038664	18q11
myeloid antigen CD15/fucosyltransferase 4/CD15	104230	NM_002033	11q21
monocyte antigen CD87/plasminogen activator receptor, urokinase type/PLAUR/CD87	173391	NM_002659	19q13
lymphocyte antigen CD10/membrane metalloendopeptidase/MME/CD10	120520	NM_000902	3q21-q27
leukocyte antigen CD13/alanyl aminopeptidase/ANPEP/CD13	151530	NM_001150	15q25-q26
chymase 1, mast cell/CMA1	118938	NM_001836	14q11.2
tryptase alpha/TPS1	191080	NM_003293	Chr.16
matrix metalloproteinase 1 (interstitial collagenase)/MMP1	120353	NM_002421	11q22-q23
matrix metalloproteinase-like 1/MMPL1	*****	NM_004142	*****
matrix metalloproteinase 2 (neutrophil gelatinase)/CLG4/MMP2	120360	AH002654	16q13
matrix metalloproteinase 3 (stromelysin 1, progelatinase)/MMP3	185250	NM_002422	11q23
matrix metalloproteinase 8 (neutrophil collagenase)/MMP8	120355	NM_002424	11q21-q22
matrix metalloproteinase 9 (gelatinase B, 92kD gelatinase, 92kD type IV collagenase)/MMP9	120361	NM_004994	10q11.2-q13.1
matrix metalloproteinase 10 (stromelysin 2)/MMP10	185260	NM_002425	11q22.3-q23

Proteases

Proteases and Inhibitors	matrix metalloproteinase 11 (stromelysin 3)/MMP11	185261	NM_005940	22q11.2
	matrix metalloproteinase 12 (macrophage elastase)/MMP12	601046	NM_002426	1q22.2-q22.3
	matrix metalloproteinase 13 (collagenase 3)/MMP13	600108	NM_002427	11q22.3
	matrix metalloproteinase 14 (membrane-inserted)/MMP14	600754	NM_004995	14q11-q12
	matrix metalloproteinase 15 (membrane-inserted)/MMP15	602261	NM_002428	16q13-q21
	matrix metalloproteinase 16 (membrane-inserted)/MMP16	602262	NM_005941	8q21
	matrix metalloproteinase 17 (membrane-inserted)/MMP17	602285	NM_004141	12q24.33
	matrix metalloproteinase 19/MMP19	601807	NM_002429	12q14
	matrix metalloproteinase 23A/MMP23A	603320	NM_004659	1p36.3
	matrix metalloproteinase 23B/MMP23B	603321	NM_006983	1p36.3
	matrix metalloproteinase 24 (membrane-inserted)/MMP24	*****	NM_006690	*****
	tryptase beta/TPS2	191081	NM_003294	Chr.16
	tissue inhibitor of metalloproteinase 1/erythroid potentiating activity/EPA/human collagenase inhibitor/HCI/TIMP1	305370	NM_003254	Xp11.3- p11.23
	secretory leukocyte protease inhibitor (antileukoproteinase)/SLPI	107285	NM_003064	*****
	Inhibitors			

			monocyte/neutrophil elastase inhibitor/ELANH2	130135	M93056	6pter-p24
			alpha-1-microglobulin/bikunin precursor/AMBP	176870	NM_001633	9q32-q33
			alpha-2-macroglobulin/A2M	103950	NM_000014	2p13.3-p12.3
Cell-Mediated Pathogen Defense	Phagocytosis of Pathogens	Scavenger Receptors	CD36/thrombospondin receptor/platelet collagen	173510	NM_000072	7q11.2
			CD36 antigen (collagen type I receptor, thrombospondin receptor)-like 1/CD36L1/SRB1	601040	NM_005505	Chr. 12
			CD5 antigen-like (scavenger receptor cysteine rich family)/CD5L	602592	NM_005894	1q21-q23
			acetyl LDL receptor/scavenger receptor expressed by endothelial	*****	NM_003693	*****
			macrophage scavenger receptor 1/MSR1	153622	NM_002445	8p22
			macrophage scavenger receptor 1-like/MSRL1	602728	*****	8p21
			mannose receptor, C type 1/MRC1	153618	NM_002438	10p13
			endocytic receptor (macrophage mannose receptor family) (KIAA0709)	*****	NM_006039	*****
			toll-like receptor 1/TLR1	601194	NM_003263	4p14
			toll-like receptor 2/TLR2	603028	NM_003264	4q32
			toll-like receptor 3/TLR3	603029	NM_003265	4q35
			toll-like receptor 4/TLR4	603030	NM_003266	9q32-q33
			toll-like receptor 5/TLR5	603031	NM_006068	1q41-q42
			collectin 34	*****	AB002631	*****
			liver collectin 1/CL-L1	*****	NM_006438	*****
			collectin receptor/complement component C1q receptor/C1QR	120577	*****	

			surfactant, pulmonary-associated protein D/SFTPD	178635	NM_003019	10q23.3
			surfactant, pulmonary-associated protein A1/SFTPA1	178630	NM_005411	0q22.2-q23.1
Immunoglobulin Light Chains	Kappa Light Chain		immunoglobulin K light chain constant region locus/IGKC	147200	*****	2p12
			immunoglobulin K light chain variable region locus/IGKV	146980	K01322	2p12
			immunoglobulin K light chain joining region locus/IGKJ	146970	*****	2p12
	Lambda Light Chain		immunoglobulin L light chain constant region locus/IGLC1	147220	NM_006146	22q11.2
			immunoglobulin L light chain joining region locus/IGLJ	147230	NM_006146	22q11.2
			immunoglobulin L light chain variable region locus/IGLJ	147240	NM_006146	22q11.2
	IgA Heavy Chain Constant Region		immunoglobulin A heavy chain constant region locus 1/IGHA1	146900	*****	14q32.33
			immunoglobulin A heavy chain constant region locus 2/IGHA2	147000	*****	14q32.33
	IgD Heavy Chain Constant Region Locus					
			immunoglobulin D heavy chain constant region locus/IGHD	147170	*****	14q32.33

Immunoglobulin Heavy Chains	IgE Heavy Chain Constant Region Locus	immunoglobulin E heavy chain constant region locus/IGHE	147180	*****	14q32.33
	IgG Heavy Chain Constant Region Locus	immunoglobulin G heavy chain constant region locus 1/IGHG1	147100	*****	14q32.33
		immunoglobulin G heavy chain constant region locus 2/IGHG2	147110	*****	14q32.33
		immunoglobulin G heavy chain constant region locus 3/IGHG3	147120	*****	14q32.33
		immunoglobulin G heavy chain constant region locus 4/IGHG4	147130	*****	14q32.33
Immunoglobulin Light Chains	IgM Heavy Chain Constant Region Locus	immunoglobulin M heavy chain constant region locus/IGHM	147020	*****	14q32.33
	Heavy Chain Variable Region Locus	immunoglobulin heavy chain variable region locus 1/IGHV1	147070	X92279	14q32.33
		immunoglobulin heavy chain variable region locus 2/IGHV2	600949	*****	16p11
	Heavy Chain Diversity Region Locus	immunoglobulin heavy chain diversity region locus 1/IGHDY1	146910	X97051	14q32.33
		immunoglobulin heavy chain diversity region locus 2/IGHDY2	146990	L25544	15q11-q12

Immunoglobulin Gene Rearrangement	Heavy Chain Joining Region Locus	immunoglobulin heavy chain joining region locus/IGHJ	147010	*****	14q32.33
	Signaling	recombination activating gene 1/RAG1	179615	NM_000448	11p13
		recombination activating gene 2/RAG2	179616	M94633	11p13
		immunoglobulin kappa J region recombination signal binding protein/RBPJK/IGKJRB1	147183	L07872	9p13-p12
		Bruton agammaglobulinemia tyrosine kinase/BTK	300300	NM_000061	Xq21.3-q22
		interleukin 7 receptor/IL7R	146661	NM_002185	5p13
		interferon-gamma receptor 1/IFNGR1	107470	NM_000416	6q23-q24
		interferon-gamma receptor 2/IFNGR2	147569	NM_005534	21q22.1-q22.2
		interleukin 4 receptor precursor/IL4R	147781	NM_000418	16p12.1-p11.2
		interleukin 4 receptor precursor/IL4R	147781	NM_000418	16p12.1-p11.2
		ligase I, DNA, ATP-dependent/LIG1	126391	NM_000234	19q13.2-q13.3
		ligase IV, DNA, ATP-dependent/LIG4	601837	NM_002312	13q22-q34
	Recombination	X-ray repair, complementing defect in Chinese hamster/Ku antigen, 80 kD/KU80/XRCC5	194364	*****	2q35

Immunoglobulin Gene Transcription Factors	thyroid autoantigen, 70 kD/KU7C/G22P1	152690	NM_001469	22q11-q13
	nuclear factor kappa-B DNA binding subunit 1/NFKB1	164011	M58603	4q23-q24
	nuclear factor kappa-B DNA binding subunit 2/NFKB2	164012	NM_002502	10q24
	nuclear factor kappa-B subunit 3/NFKB3	164014	Z22949	11q12-q13
	nuclear factor of kappa light chain gene enhancer in B cells, inhibitor alpha/NFKBIA	164008	*****	14q13
	nuclear factor of kappa light chain gene enhancer in B cells, inhibitor beta/NFKBIB	603258	NM_002503	8p11.2
	YY1 transcription factor/YY1	600013	NM_003403	14q
	immunoglobulin transcription factor 1/ITF1/transcription factor 3/TCF3	147141	*****	19p13.3
	immunoglobulin transcription factor 2/ITF2/transcription factor 4/TCF4	602272	NM_003199	18q21.1
	immunoglobulin mu binding protein 2/IGHMBP2	600502	NM_002180	11q13.2-q13.4
	transcription factor binding to IGHM enhancer 3/TFE3	314310	NM_006521	Xp11.22
	homeobox protein OCT1/POU domain transcription factor 2, class 1/POU2F1	164175	NM_002697	1q22-q23
	homeobox protein OCT2/POU domain transcription factor 2, class 2/POU2F2	164176	M22596	Chr.19
	POU domain, class 2, associating factor 1/POU2AF1	601206	NM_006235	11q23.1

			inhibitor of DNA binding 1, dominant negative helix-loop-helix protein/ID1	600349	NM_002165	20q11
			inhibitor of DNA binding 2, dominant negative helix-loop-helix protein/ID2	600386	NM_002166	2p25
Immunoglobulin Isotype Switching	Signaling		B-cell antigen CD40/tumor necrosis factor receptor superfamily, member 5/CD40/TNFRSF5	109535	NM_001250	20q12-q13.2
			paired box gene 5/B-cell lineage-specific activator protein/BSAP/PAX5	167414	*****	9p13
			lymphocyte function-associated antigen, type 3/LFA3/LEU7/CD58	153420	NM_001779	1p13
			interleukin 10 receptor, alpha/IL10RA	146933	NM_001558	11q23.3
			lymphocyte antigen CD45/protein tyrosine phosphatase, receptor type, c polypeptide/PTPRC/CD45	151460	NM_002838	1q31-q32
			prostaglandin E receptor 1, EP1 subtype/PTGER1	176802	NM_000955	19p13.1
			prostaglandin E receptor 2, EP2 subtype/PTGER2	176804	*****	5p13.1
			prostaglandin E receptor 3, EP3 subtype/PTGER3	176806	NM_000957	1p31.2
			prostaglandin E receptor 4, EP4 subtype/PTGER4	601586	NM_000958	5p13.1
			interleukin 13 receptor, alpha 1/IL13RA1	300119	NM_001560	Chr.X
			interleukin receptor 13 alpha2/IL13A2	300130	X95302	Xq24
			interferon-gamma receptor 1/IFNGR1	107470	NM_000416	6q23-q24

Defense Proteins and Peptides	interferon-gamma receptor 2/IFNGR2	147569	NM_00553 4	21q22.1- q22.2
	interleukin 5 receptor alpha/IL5RA	147851	M96652	3p26-p24:
	transforming growth factor, beta receptor I (activin A receptor type II- like kinase, 53kD)/TGFBRI	190181	NM_00461 2	9q33-q34
	transforming growth factor, beta receptor II (70-80kD)/TGFBRII	190182	NM_00324 2	3p22
	transforming growth factor, beta receptor III (betaglycan, 300kD)/TGFBRIII	600742	NM_00324 3	1p33-p32
	X-ray repair, complementing defect in Chinese hamster/Ku antigen, 80 kD/KU80/XRCC5	194364	*****	2q35
	thyroid autoantigen, 70 kD/KU70/G22P1	152690	NM_00146 9	22q11-q13
	complement component 1, R subcomponent/C1R	216950	NM_00173 3	12p13
	complement component 1, S subcomponent/C1S	120580	NM_00173 4	12p13
	complement component 1, Q subcomponent, alpha polypeptide/C1QA	120550	*****	1p36.3- p34.1
Recombination	complement component 1, Q subcomponent, beta polypeptide/C1QB	120570	*****	1p36.3- p34.1
	complement component 1, Q subcomponent, gamma polypeptide/C1QG	120575	*****	1p36.3- p34.1
	complement component 1, Q subcomponent binding protein/C1QBP	601269	NM_00121 2	17p13.3

complement component 1 inhibitor (angioedema, hereditary) /C1NH	106100	NM_00006 2	11q11- q13.1
complement component 2/C2	217000	NM_00006 3	6p21.3
complement component 3/C3	120700	NM_00006 4	19p13.3- p13.2
complement component 4B/C4B	120820	NM_00059 2	6p21.3
complement component 5/C5	120900	NM_00173 5	9q34.1
complement component 6/C6	217050	NM_00006 5	5p13
complement component 7/C7	217070	NM_00058 7	5p13
complement component 8, alpha polypeptide/C8A	120950	NM_00056 2	1p32
complement component 8, beta polypeptide/C8B	120960	NM_00006 6	1p32
complement component 8, gamma polypeptide/C8G	120930	NM_00060 6	9q34.3
complement component 9/C9	120940	NM_00173 7	5p13
complement factor H/H factor 1/HF1	134370	NM_00018 6	1q32
I factor (complement)/IF	217030	NM_00020 4	4q25
decay-accelerating factor for complement/DAF/CD55	125240	S72858	1q32
perforin 1/preforming protein/PRF1	170280	NM_00504 1	10q22

**Classical
Pathway**

Complement

leukocyte antigen p18-20/protectin/CD59	107271	M95708	11p13
T-cell antigen CD46/membrane cofactor protein/MCP/measels virus receptor/CD46	120920	Y07713	1q32
erythrocyte antigen CD55/decay-accelerating factor for complement/DAF/CD55	125240	S72858	1q32
leukocyte antigen p18-20/protectin/CD59	107271	M95708	11p13
erythrocyte antigen CD35/complement receptor CR1 (receptor for components C3b/C4b)/CD35/CR1	120620	AH002679	1q32
complement component 3a receptor 1/C3AR1	*****	NM_004054	*****
complement component 4-binding protein, alpha/C4BPA	120830	NM_000715	1q32
complement component 4-binding protein, beta/C4BPB	120831	NM_000716	1q32
complement component 5 receptor 1 (C5a ligand)/C5AR1	113995	NM_001736	Chr.19
antigen CD21/CD21	*****	X98257	*****
Alternative Pathway	B-factor, properdin/BF	NM_001710	6p21.3
	properdin P factor, complement/PFC	NM_002621	Xp11.4-p11.23
	adipsin/complement factor D precursor/DF	NM_001928	*****

Defensins and Related Protective Proteins	defensin, alpha 1, myeloid-related sequence/DEFA1	125220	NM_004084	8p23.2-p23.1
	defensin, alpha 3, neutrophil-specific/DEFA3	*****	NM_005217	*****
	defensin, alpha 4/corticostatin/DEFA4	601157	NM_001925	Chr.8
	defensin, alpha 5/DEFA5	600472	M97925	8pter-p21
	defensin, alpha 6, Paneth cell-specific/DEFA6	600471	NM_001926	8pter-p21
	defensin, beta 1/DEFB1	602056	NM_005218	8p23.2-p23.1
	defensin, beta 2/DEFB2	602215	NM_004942	8p23.1-p22
	ribonuclease, RNase A family, 2/eosinophil-derived neurotoxin/EDN/RNASE2	131410	NM_002934	14q24-q31
	ribonuclease, RNase A family, 3/eosinophil cationic protein/ECP/RNASE3	31398	NM_002935	14q24-q31
	myeloperoxidase/MPO	254600	J02694	17q23.1
	eosinophil peroxidase/EPX	131399	NM_000502	*****
	cathelicidin antimicrobial peptide/CAMP	600474	NM_004345	3p21.3
	lysozyme/LYZ	153450	NM_000239	Chr.12
	chitinase 1/CHIT1	600031	NM_003465	1q31-q32
	lactotransferrin/LTF	150210	NM_002343	3q21-q23
Acute Protection				

II VIII Pathogens	polyadenylate binding protein/TIA1	603518	M77142	2p13
	TIA1 cytotoxic granule-associated RNA-binding protein-like 1/TIAL1	603413	NM_003252	10q
	granulysin/NKG5	603082	NM_006433	2p12-q11
	neutrophil azurocidin/NAZC	162815	M96326	19p13.3
	bactericidal/permeability-increasing protein precursor/BPI	109195	NM_001725	20q11.23-q12
	lipopolysaccharide-binding protein/LBP	151990	AF105067	20q11.23-q12
	monocyte antigen CD14/monocyte differentiation antigen/CD14	158120	NM_000591	5q31.1
	proteoglycan 1, secretory granule/serglycin/PRG1	177040	NM_002727	10q22.1
	proteoglycan 2, bone marrow/natural killer cell activator, eosinophil granule major basic protein/PRG2	*****	NM_002728	*****
	prepro-major basic protein homolog/MBPH	*****	NM_006093	*****
	neuronal pentraxin I/NPTX1	602367	NM_002522	17q25.1-q25.2
	neuronal pentraxin II/NPTX2	600750	U26662	7q21.3-q22.1
	pentraxin-related gene, rapidly induced by IL-1 beta/PTX3	602492	NM_002852	3q25
	amyloid P component, serum/APCS	104770	NM_001639	1q21-q23
	C-reactive protein, pentraxin-related/CRP	123260	X56214	1q21-q23

Pentraxins

Degranulation of Platelets, Mast Cells, Neutrophils, and Eosinophils	Receptors	mast cell IgE receptor alpha polypeptide/FCER1A	147140	*****	1q23
		mast cell IgE receptor beta polypeptide/FCER1B	147138	NM_000139	11q13
		mast cell IgE receptor beta polypeptide/FCER1G	147139	NM_004106	1q23
		granulocyte antigen CD62/platelet alpha-granule membrane protein/selectin P/CD62/SELP	173610	NM_003005	1q23-q25
		neutrophil antigen CD16/low-affinity receptor IIIA for Fc fragment of IgG/FCGR3A/CD16	146740	M24853	1q23
		prostaglandin I2 receptor/PTGIR/prostacyclin receptor	600022	SEG_HUMI	19q13.3
		formyl peptide receptor 1/FPR1	136537	NM_002029	Chr.19
		formyl peptide receptor-like 1/FPRL1	136538	NM_001462	19q13.3-q13.4
		formyl peptide receptor-like 2/FPRL2	136539	NM_002030	19q13.3-q13.4
		lipoxin A4 receptor	*****	AF054013	*****
	Signaling	inositol polyphosphate-5-phosphatase, 145 kD/SH2-containing inositol 5-phosphatase/SHIP/INPP5D	601582	NM_005541	2q36-q37
		v-src-1 Yamaguchi sarcoma viral related oncogene homolog/LYN	165120	NM_002350	8q13-qter
		guanine nucleotide binding protein (G protein), q polypeptide/GNAQ	600998	NM_002072	9q21

		guanine nucleotide binding protein (G protein), alpha inhibiting activity, polypeptide 2/GNAI2	139360	NM_002070	3p21
Release of Membrane Lipids (common to PAF, lipoxin, leukotriene, and prostaglandin pathways)	Phospholipases	phospholipase A2 group	172411	NM_000300	1p35
		phospholipase A2 group IB/PLA2G1B	172410	NM_000928	12q23-q24.1
		phospholipase A2 group X/PLA2G10	603603	NM_003561	16p13.1-p12
		phospholipase A2 group IVA/PLA2G4A	600522	U08374	1q25
		phospholipase A2 group VI/PLA2G6	603604	AF064594	22q13.1
		phospholipase A2 group IVC/PLA2G4C	603602	NM_003706	chr. 19
		phospholipase A2 group V/PLA2G5	601192	NM_000929	1p36-p34
		phospholipase C, beta 2/PLCB2	604114	NM_004573	15q15
		phospholipase C, beta 3/PLCB3	600230	U26425	11q13
		phospholipase C, beta 4/PLCB4	600810	NM_000933	20p12
		phospholipase C, delta 1/PLCD1	602142	NM_006225	3p22-p21.3
		phospholipase C, epsilon/PLCE	600597	NM_006226	2q33
		phospholipase C, gamma 1 (formerly subtype 148)/PLCG1	172420	NM_002660	20q12-q13.1
		phospholipase C, gamma 2 (phosphatidylinositol-specific)/PLCG2	600220	NM_002661	16q24.1
		lysosomal acid lipase/LIPB	278000	NM_000235	10q24-q25
	Annexins	lipocortin 1/annexin 1/ANXA1	151690	V00546	9q11-q22
		lipocortin 2/annexin 2/ANXA2	151740	D00017	15q21-q22
		lipocortin 3/annexin 3/ANXA3	106490	M20560	4q21
		lipocortin 5/annexin 5/ANXA4	131230	NM_001154	4q26-q28
		lipocortin 7/annexin 7/ANXA1	186360	NM_004034	10q21.1-q21.2

Arachidonate Metabolism	arachidonate 12-lipoxygenase, 12R type/ALOX12B	603741	NM_001139	17pter-p13.1
	arachidonate 15-lipoxygenase/ALOX15	152392	NM_001140	17p13.3
	arachidonate 15-lipoxygenase, second type/ALOX15B	603697	NM_001141	*****
	prostaglandin endoperoxide synthetase 1/COX1/PTGS1	176805	AH001520	9q32-q33.3
Biosynthesis	prostaglandin endoperoxide synthetase 2/COX2/PTGS2	600262	NM_000963	1q25.2-q25.3
	thromboxane A synthase 1/TBXAS1	274180	EG_D34613	7q34
	prostaglandin D2 synthase (hematopoietic)	602598	*****	*****
	prostaglandin D2 synthase (21kD, brain)/PTGDS	176803	M61900	*****
	prostaglandin I2 synthase/prostacyclin synthase/PTGIS	601699	EG_D83393	20q13
	prostaglandin E receptor 1, EP1 subtype/PTGER1	176802	NM_000955	19p13.1
Prostaglandins	prostaglandin E receptor 2, EP2 subtype/PTGER2	176804	*****	5p13.1
	prostaglandin E receptor 3, EP3 subtype/PTGER3	176806	NM_000957	1p31.2
	prostaglandin E receptor 4, EP4 subtype/PTGER4	601586	NM_000958	5p13.1
	prostaglandin F receptor/PTGFR	600563	L24470	1p31.1
	prostaglandin F2 receptor negative regulator/PTGFRN	601204	U26664	1p13.1-q21.3
	Receptors			

Small Molecule Mediators of Inflammation		prostaglandin I2 receptor/PTGIR/prostacyclin receptor solute carrier family 21 (prostaglandin transporter), member 2/SLC21A2	600022	SEG_HUMI	19q13.3
			601460	NM_005630	3q21
			601688	NM_000860	4q34-q35
	Catabolism	15-hydroxyprostaglandin dehydrogenase/HPGD	600450	NM_001353	10p15-p14
		aldo-keto reductase family 1, member C2/AKR1C2	*****	*****	*****
	Biosynthesis	CDP-choline:alkylacetyl glycerol cholinephosphotransferase	173393	M88177	1p35-p34.3
	Receptors	platelet activating factor receptor/PTAFR	601690	NM_005084	6p21.2-p12
	Catabolism	platelet activating factor acetylhydrolase 1/PAFAH1	601545	NM_000430	17p13.3
		platelet activating factor acetylhydrolase, isoform 1B, alpha	602508	NM_002572	11q23
		platelet activating factor acetylhydrolase, isoform 1B, beta	603074	NM_002573	19q13.1
		platelet activating factor acetylhydrolase, isoform 1B, gamma	602344	NM_000437	*****
		platelet activating factor acetylhydrolase 2/PAFAH2	152390	NM_000698	Chr.10
		arachidonate 5-lipoxygenase/ALOX5	603700	NM_001629	13q12
	Biosynthesis	arachidonate 5-lipoxygenase- activating protein/FLAP/ALOX5AP	603741	NM_001139	17pter- p13.1

Lipoxins	Gamma-glutamyltranspeptidase 1/GGT1	231950	J04131	22q11.1- q11.2
	Gamma-glutamyltranspeptidase 2/GGT2	137181	AH002728	22q11.1
	Gamma-glutamyltransferase-like activity 1/GGTLA1	137168	NM_00412 1	*****
	Receptors	*****	AF054013	*****
Leukotrienes	Catabolism			
	renal microsomal dipeptidase/DPEP1	179780	NM_00441 3	16q24.3
	arachidonate 5-lipoxygenase/ALOX5	152390	NM_00069 8	Chr.10
	arachidonate 5-lipoxygenase- activating protein/FLAP/ALOX5AP	603700	NM_00162 9	13q12
	leukotriene A4 hydrolase/LTA4H (aminopeptidase)	151570	NM_00089 5	12q22
	leukotriene C4 synthase/LTC4S	246530	NM_00089 7	5q35
	Gamma-glutamyltranspeptidase 1/GGT1	231950	J04131	22q11.1- q11.2
	Gamma-glutamyltranspeptidase 2/GGT2	137181	AH002728	22q11.1
	Gamma-glutamyltransferase-like activity 1/GGTLA1	137168	NM_00412 1	*****
	Receptors			
	cysteinyl leukotriene receptor 1/CYSLT1	300201	NM_00663 9	Xq13-q21
	leukotriene b4 receptor (chemokine receptor-like 1)/LTB4R	601531	NM_00075 2	14q11.2- q12
	Catabolism			
	renal microsomal dipeptidase/DPEP1	179780	NM_00441 3	16q24.3
Biosynthesis	Histidine Decarboxylase	142704	M60445	15q21-q22

Histamine	Receptors	histamine H1 receptor/HRH1	600167	NM_000861	3p21-p14
		histamine H2 receptor/HRH2	142703	AB023486	*****
		histamine H3 receptor/HRH3	*****	NM_007232	*****
	Catabolism	Histamine N-methyltransferase	*****	D16224	chr. 2
		Amine oxidase (copper-containing) 2/AOC2	602268	D88213	17q21
		Amine oxidase (copper-containing) 3/AOC3	603735	AF054985	17q21
	Synthesis	aromatic L-Amino Acid			
		Decarboxylase/AADC	107930	M76180	7p11
		tryptophan hydroxylase/TPH	191060	X52836	11p15.3-p14
		14-3-3 protein ETA	113508	X78138	22q12
		14-3-3 protein ZETA	601288	M86400	2p25.2-p25.1
		14-3-3 protein BETA	601289	X57346	20q13.1
Serotonin	Receptors	14-3-3 protein SIGMA	601290	X57348	*****
		serotonin 5-HT receptors 5-HT1A, G protein-coupled	109760	X57829	5q11.2-q13
		serotonin 5-HT receptors 5-HT1B, G protein-coupled	182131	M81590	6q13
		serotonin 5-HT receptors 5-HT1C, G protein-coupled	312861	U49516	Xq24
		serotonin 5-HT receptors 5-HT1D, G protein-coupled	182133	M81590	1p36.3-p34.3
		serotonin 5-HT receptors 5-HT1E, G protein-coupled	182132	M91467	6q14-q15
		serotonin 5-HT receptors 5-HT1F, G protein-coupled	182134	L05597	3p12

		serotonin 5-HT receptors 5-HT2A, G protein-coupled	182135	D87030	13q14-q21
		serotonin 5-HT receptors 5-HT2B, G protein-coupled	601122	X77307	2q36.3-q37.1
		serotonin 5-HT receptors 5-HT2C, G protein-coupled	312861	U49516	Xq24
		serotonin transporter	182138	X70697	17q11.1-q12
	Catabolism	monoamine oxidase A/MAOA	309850	M69226	Xp11.23
		monoamine oxidase B/MAOB	309860	M69177	Xp11.23
		serotonin N-Acetyltransferase/SNAT	600950	U40347	17q25
		tryptophan 2,3-dioxygenase/TDO2	191070	NM_005651	4q31-q32
Nitric Oxide Pathway	Synthesis	nitric oxide synthetase 1/NOS1	163731	AH001515	12q24.2-q24.31
		nitric oxide synthetase 2A/NOS2A	163730	X85766	17cen-q11.2
		macrophage nitric oxide synthetase 2B/NOS2B	600719	AH006623	17p13.1-q25
		macrophage nitric oxide synthetase 2C/NOS2C	600720	600720	17p13.1-q25
		nitric oxide synthetase 3/NOS3	163729	AH001515	7q36
		chondrocyte nitric oxide synthetase 3/NOS4	163728	X73029	*****
		arginase/ARG1	207800	NM_000045	*****
		arginase/ARG2	107830	NM_001172	14q24.1-q24.3
		endothelin 1/EDN1	131240	NM_001955	6p24-p23
		endothelin 2/EDN2	131241	NM_001956	1p34
	Synthesis	endothelin 3/EDN3	131242	NM_000114	10q13.2-q13.3

Vascularization	Endothelin	endothelin converting enzyme 1/ECE1	600423	NM_001397	1p36.1
	Receptor	endothelin A receptor isoform delta 3/EDNRA	131243	AF014826	Chr.4
Vascular Endothelial Growth Factor	Synthesis	endothelin receptor type B/EDNRB	131244	NM_000115	13q22
		vascular endothelial growth factor A/VEGFA	192240	M32977	6p12
		vascular endothelial growth factor B/VEGFB	601398	U52819	11q13
		vascular endothelial growth factor C/VEGFC	601528	X94216	*****
	Receptor	VEGF receptor	191306	X61656	4q12
	Synthesis	dopamine beta hydroxylase/DBH	223360	Y00096	9q34
		phenylethanolamine-N-methyltransferase/PNMT	171190	NM_002686	17q21-q22
	Receptors	tyrosine hydroxylase/TH	191290	X05290	11p15.5
		alpha-1a-adrenergic	104219	M76446	Chr.20
		alpha-1b-adrenergic	104220	L31773	5q33
		alpha-1c-adrenergic	104221	D25235	8p21
		alpha-1d-adrenergic	104222	M76446	20p13
		alpha-2a-adrenergic	104210	M18415	10q24-q26
		alpha-2b-adrenergic	104260	AF005900	Chr.2
		alpha-2c-adrenergic	104250	J03853	4q16.1
		beta-1-adrenergic receptor/ADRB1	109630	J03019	10q24-q26
		Beta-2-Adrenergic Receptor/ADRB2	109690	M15169	5q32-q34
		beta-adrenergic receptor kinase 1/BARK1	109635	NM_001619	11cen-q13
		Beta-2-Adrenergic Receptor-Like Protein G-21/ADRB2L	109760	X57829	5q11.2-q13
		Beta-3-Adrenergic Receptor/ADRB3	109691	X70811	8p12-p11.2

Epinephrine and Norepinephrine	Beta-Adrenergic Receptor Kinase 1/ADRBK1	109635	X61157	11cen-q13
	Beta-Adrenergic Receptor Kinase 2/ADRBK2	109636	X69117	22q11
Response	phosphodiesterase 4A, cAMP- specific/PDE4A	600126	NM_00620 2	19p13.2
	phosphodiesterase 4B, cAMP- specific/PDE4B	600127	NM_00260 0	1p31
	phosphodiesterase 4C, cAMP- specific/PDE4C	600128	*****	Chr.19
	phosphodiesterase 4D, cAMP- specific/PDE4D	600129	NM_00620 3	5q12
	phosphodiesterase 7A, cAMP- specific/PDE7A	171885	L12052	8q13-q22
	phosphodiesterase 8A, cAMP- specific/PDE8A	602972	AF056490	*****
	phosphodiesterase 9A, cAMP- specific/PDE9A	602973	NM_00260 6	21q22.3
	Vesicular Amine Transporter 2/VAT2	193001	L09118	10q25
	Vesicular Amine Transporter 1/VAT1	193002	*****	8p21.3
	Solute carrier family 6, member 5/SLC6A2/NAT1/NET1	163970	NM_00104 3	16q12.2
Catabolism	Monoamine Oxidase A/MAOA	309850	M69226	Xp11.23
	Monoamine Oxidase B/MAOB	309860	M69177	Xp11.23
	Catechol-O-Methyltransferase/COMT	116790	M58525	22q11.2
Biosynthesis	Aromatic L-Amino Acid Decarboxylase/AADC/dopa decarboxylase	107930	M76180	7p11
	Tyrosine Hydroxylase	191290	X05290	11p15.5

Dopamine	Receptors	Dopamine Receptor D1	126449	X58987	5q35.1
		Dopamine Receptor D2/DRD2	126450	NM_000795	11q23
		Dopamine Receptor D3/DRD3	126451	U32499	3q13.3
		Dopamine Receptor D4	126452	L12398	11p15.5
		Dopamine Receptor D5	126453	M67439	4p16.1-p15.3
	Reuptake	Dopamine Transporter/ DAT1	126455	L24178	5p15.3
	Catabolism	Dopamine Beta-Hydroxylase/monooxygenase	223360	Y00096	9q34
		Catechol-O-Methyltransferase	116790	M58525	22q11.2
		Monoamine Oxidases A	309850	M69226	Xp11.23
		Monoamine Oxidases B	309860	M69177	Xp11.23
		Phenol Sulfotransferase 1	171150	L10819	16p12.1-p11.2
		Phenol Sulfotransferase 2	601292	X78282	16p12.1-p11.2
		Phenol Sulfotransferase 3	600641	L19956	16p11.2
	Biosynthesis	adenylosuccinate lyase/ADSL	103050	NM_000026	22q13.1
		adenylosuccinate synthetase/ADSS	103060	NM_001126	1cen-q12
		Adenosine A1 Receptor; Adora1/G protein-coupled	102775	L22214	1q32.1
		Adenosine A2 Receptor; Adora2a/G protein-coupled	102776	X68486	22q11.2
		Adenosine A2b Receptor; Adora2b/G protein-coupled	600446	X68487	17p12-p11.2
		Adenosine A3 Receptor; Adora3/G protein-coupled	600445	L20463	1p21-p13

Adenosine	Receptors	Adenosine A2 Receptor-like/ADORA2L1	102777	*****	10q25.3-q26.1
		Purinergic Receptor P2x, Ligand-Gated Ion Channel, 1; P2rx1	600845	NM_002558	*****
		Purinergic Receptor P2x, Ligand-Gated Ion Channel, 3; P2rx3	600843	Y07683	11q12
		Purinergic Receptor P2x, Ligand-Gated Ion Channel, 4; P2rx4	600846	AF000234	12q24.32
		Purinergic Receptor P2x, Ligand-Gated Ion Channel, 5; P2rx5	602836	NM_002561	*****
		Purinergic Receptor P2x, Ligand-Gated Ion Channel, 7; P2rx7	602566	Y09561	12q24
		P2Y11 purinoceptor/G protein-receptor/G protein-coupled	602697	*****	*****
		P2Y7 purinoceptor/leukotriene B4 receptor/G protein-coupled	601531	NM_000752	14q11.2-q12
		P2Y2 purinoceptor/G protein-coupled	600041	U07225	1q13.5-q14.1
		P2Y1 purinoceptor/G protein-coupled	601167	U42029	3q25
		P2Y4 pyrimidinergic receptor/G protein-coupled	300038	NM_002565	Xq13
		P2Y6 pyrimidinergic receptor/G protein-coupled	602451	NM_004154	11q13.5
Reuptake	Solute carrier family 29 (nucleosides), member 1/SLC29A1/ENT1	602193	NM_004955	6p21.2-p21.1	
	Solute carrier family 29 (nucleosides), member 2/SLC29A2/ENT2	602110	X86681	11q13	
Catabolism	adenosine deaminase	102700	NM_000022	20q13.11	
Biosynthesis	Choline acetyltransferase/CHAT	118490	NM_003055	10q11.2	
	carnitine acetyltransferase/CRAT	600184	NM_004003	9q34.1	
	apolipoprotein E	107741	NM_000041	19q13.2	

Neurotransmitter and Peptide Hormone Inflammatory Modulation	Acetylcholine	Receptors				
		Cholinergic Receptor, Muscarinic, 1; CHRM1	118510	X15263	11q13	
		Cholinergic Receptor, Muscarinic, 2; CHRM2	118493	U19800	7q35-q36	
		Cholinergic Receptor, Muscarinic, 3; CHRM3	118494	U29589	1q41-q44	
		Cholinergic Receptor, Muscarinic, 4; CHRM4	118495	M16405	11p12-p11.2	
		Cholinergic Receptor, Muscarinic, 5; CHRM5	118496	AF026263	15q26	
		Nicotinic, Cholinergic receptor alpha 1	100690	X70108	2q24-q32	
		Nicotinic, Cholinergic receptor alpha 2	118502	U62431	Chr.8	
		Nicotinic, Cholinergic receptor alpha 3	118503	X53559	15q24	
		Nicotinic, Cholinergic receptor alpha 4	118504	U62433	20q13.2-q13.3	
		Nicotinic, Cholinergic receptor alpha 5	118505	M83712	15q24	
		Nicotinic, Cholinergic receptor alpha 7/CHRNA7	118511	U40583	15q14	
		Nicotinic, Cholinergic receptor beta 1	100710	X14830	17p12-p11	
		Nicotinic, Cholinergic receptor beta 2	118507	Y08415	1p21	
		Nicotinic, Cholinergic receptor beta 3	118508	X67513	8p11.2	
		Nicotinic, Cholinergic receptor beta 4	118509	X68275	15q24	
		Nicotinic, Cholinergic receptor epsilon polypeptide	100725	X66403	Chr.17	
		Nicotinic, Cholinergic receptor,	100720	X55019	2q33-q34	
		Nicotinic, Cholinergic receptor,	100730	NM_005199	2q33-q34	
		Vesicular acetylcholine transporter	600336	NM_003055	10q11.2	
		Acetylcholinesterase/ACHE	100740	M55040	7q22	
		Catabolism	butyrylcholinesterase 1/serum			
			cholinesterase 1/BCHE1	177400	NM_000053	26.1-q26.2

4czf01_.xls

Potassium Channels	cyclic nucleotide gated hyperpolarization activated potassium	602781	AF064877	*****
	potassium inwardly-rectifying channel, subfamily J, member 2 (KCNJ2)	600681	NM_000891	Chr. 17
	voltage dependent potassium channel, subfamily K, member 2/KCNK2	603219	*****	1q41
	G protein coupled potassium channel, subfamily J, member	601534	NM_002239	2q24.1
	G protein coupled potassium channel inward rectifier/GIRK3	600932	*****	1q21-q23
	voltage dependent potassium channel, subfamily S, member 3/KCNK3	603888	AF043472	2p24
	potassium voltage-gated channel precursor, KQT-like subfamily, member 1/KCNQ1	192500	NM_000218	11p15.5
	potassium intermediate/small conductance calcium-activated channel, subfamily N, member	602754	NM_002250	19q13.2
	chloride channel, calcium activated, family member 1/CLCA1	603906	NM_001285	1p31-p22
	chloride channel, calcium activated, family member 2/CLCA2	604003	NM_006536	*****
Chloride	cystic fibrosis transmembrane conductance regulator/CFTR	602421	NM_000492	7q31.2
	membrane metalloendopeptidase/MME/neutral endopeptidase	120520	AH002677	3q21-q27
	proopiomelanocortin	176830	NM_000939	2p23.3

Opioids	Biosynthesis	prepronociceptin/nociceptin/nosistatin/ PNOC	601459	*****	8p21
		preproenkephalin			
		B/prodynorphin/PDYN	131340	NM_006211	20pter-p12.21
		preproenkephalin			
		A/proenkephalin/PENK	131330	NM_006211	8q23-q24
	Receptors	Opioid Receptor, Mu-1; Oprm1	600018	NM_000914	6q24-q25
		Opioid Receptor, Kappa-1; Oprk1	165196	U17298	8q11.2
		opioid receptor-like 1/OPRL 1	602548	X77130	*****
		Opioid Receptor, Delta-1; Oprd1	165195	U10504	1p36.1-p34.3
		Opioid Receptor, Sigma 1	601978	U75283	*****
		opioid binding cell adhesion molecule/OBCAM	600632	*****	Chr.11
		G protein-coupled receptor 7/GPR7	600730	U22491	0q11.2-q21.1
		G protein-coupled receptor 8/GPR8	600731	U22492	20q13.3
Leptin	Biosynthesis	leptin/LEP	164160	NM_000230	7q31.3
	Receptor	leptin receptor/LEPR	601007	NM_002303	1p31
	Biosynthesis	Cholecystokinin/CCK	118440	L00354	3pter-p21
	Receptors	Cholecystokinin A receptor/CCKAR	118444	L13605	4p15.2-p15.1
		Cholecystokinin B receptor/CCKBR	118445	L08112	1p15.5-p15.4
		Neurokinin A/Tachykinin 1 or 2/Substance P or K	162320	U37529	7q21-q22
	Biosynthesis	Neurokinin B/Tachykinin 3	162330	*****	12q13-q21
	Receptors	Tachykinin NK1 receptor/TACR1	162323	M81797	Chr.2
		Tachykinin NK2 receptor/TACR2	162321	M57414	10q11-q21
		Tachykinin NK3 receptor/TACR3	162332	M89473	*****
	Biosynthesis	kininogen/KNK	228960	*****	3q27
		kallikrein 1/KLK1	147910	AH002853	9q13.2-q13.4

Bradykinin	Receptor	bradykinin receptor B1/BDKRB1 G protein-coupled	600337	NM_000710	4q32.1-q32.2	
		bradykinin receptor B2/BDKRB2 G protein-coupled	113503	NM_000623	4q32.1-q32.2	
	Biosynthesis	parathyroid hormone-related protein/parathyroid hormone-like hormone/PTH	168470	NM_002820	12p12.1-p11.2	
		parathyroid hormone/PTH	168450	NM_000315	1p15.3-p15.1	
Parathyroid Hormone (PTH)	Receptors	parathyroid hormone receptor	168468	NM_000316	3p22-p21.1	
		parathyroid hormone receptor	601469	NM_005048	2q33	
	Biosynthesis	proopiomelanocortin	176830	NM_000939	2p23.3	
	ACTH		melanocortin 1 receptor (alpha melanocyte stimulating hormone receptor)/MC1R	155555	NM_002386	16q24.3
			melanocortin 2 receptor/ACTH receptor/MC2R	202200	NM_000529	18p11.2
			melanocortin 4 receptor/MC4R	155541	NM_005912	18q22
			melanocortin 5 receptor/MC5R	600042	NM_005913	18p11.2
		Receptor	Folate Receptor Alpha/FOLR1	136430	M28099	1q13.3-q13.5
			Folate Receptor Beta/FOLR2	136425	AF000380	1q13.3-q13.5
	Folate Receptor Gamma/FOLR3		602469	Z32564	*****	
Folate Transporter (SLC19A1)	600424		U19720	21q22.3		
Transporter	Vitamin B12 binding protein	275350	NM_000355	22q11.2-qter		
	Glutaminati on	folypolyglutamate synthetase/FPGS	136510	M98045	9cen-q34	
		gamma-glutamyl hydrolase/GGH	601509	U55206	*****	
		Methylenetetrahydrofolate reductase/MTHFR	236250	U09806	1p36.3	
		Dihydrofolate reductase/DHFR	126060	J00140	5q11.2-q13.2	

**Folate
Metabolism**

Metabolism

5,10-methylenetetrahydrofolate dehydrogenase, 5,10-methylenetetrahydrofolate cyclohydrolase, 10-formyltetrahydrofolate synthetase/MTHFD1	172460	NM_005956	14q24
5,10-methylenetetrahydrofolate synthetase (5-formyltetrahydrofolate cyclo-ligase)/MTHFS	604197	NM_006441	Chr. 15
phosphoribosylglycinamide formyltransferase, phosphoribosylglycinamide synthetase,			
phosphoribosylaminoimidazole folate hydrolase 1/FOH1	138440	NM_000819	21q22.1
6-pyruvoyl tetrahydrobiopterin synthase/PTPS	600934	NP_004467	11q14
serine hydroxymethyltransferase 1 (soluble)/SHMT1	261640	Q03393	1q22.3-q23.2
serine hydroxymethyltransferase 2 (mitochondrial)/SHMT2	182144	NM_004169	17p11.2
Glycine aminotransferase/glycine cleavage T protein/GAT	138450	NM_005412	12q13
5-methyltetrahydrofolate-homocysteine methyltransferase/methionine glutamate	238310	NM_000481	3p21.2-p21.1
formiminotransferase/dihydrofolate synthetase	156570	NM_000254	1q43
	229100	*****	*****

General Cell Growth	Purine Metabolism	Purine Metabolism	hypoxanthine-guanine phosphoribosyltransferase	308000	M31642	Xq26-q27.2
			adenosine phosphoribosyltransferase/APRT	102600	NM_000485	16q24
			thiopurine S-methyltransferase/TPMT	187680	NM_000367	6p22.3
			IMP (inosine monophosphate) dehydrogenase 1/IMPDH1	146690	NM_000883	7q31.3-q32
			IMP (inosine monophosphate) dehydrogenase 2/IMPDH2	146691	NM_000884	3p21.2
			adenylosuccinate synthetase/ADSS	103060	NM_001126	1cen-q12
			adenylosuccinate lyase	103050	NM_000026	22q13.1
			glycinamide ribotide formyltransferase	138440	X54199	21q22.1
			urate oxidase	191540	AH003594	1p22
			purine nucleoside phosphorylase	164050	NM_000270	14q13.1
			xanthine oxidase	278300	NM_000379	2p23-p22
			adenosine deaminase	102700	NM_000022	20q13.11
	Cytoskeleton	Tubulin	beta tubulin/TUBB	191130	NM_001069	6p21.3
			beta tubulin 2/TUBB2	602660	NM_006088	*****
			beta tubulin 4/TUBB4	602661	NM_006086	*****
			beta tubulin 5/TUBB5	602662	NM_006087	*****

		gamma tubulin/TUBG	191135	NM_001070	*****
	Oxygen Stress (additional genes in Toxicology)	superoxide dismutase 1/SOD1	147450	NM_000454	21q22.1
		superoxide dismutase 2, mitochondrial/SOD2	147460	X65965	6q25.3
		thioredoxin-dependent peroxide reductase/TDPX1	600538	NM_005809	13q12
		peptide methionine sulfoxide reductase/MSRA	601250	*****	*****
		lipoprotein, Lp(a)/LPA	152200	NM_005577	6q27
		succinate dehydrogenase complex, subunit C, integral membrane protein/SDHC	602413	NM_003001	1q21
		glucose-6-phosphate dehydrogenase/G6PD (mitochondrial)	305900	NM_000402	Xq28
		aldehyde oxidase 1/AOX1	602841	NM_001159	2q33

Table 5. Metabolism and Endocrinology Gene List

Class	Pathway	Function	Name	OMIM	GID	Locus
			membrane			
			metalloendopeptidase/neutral	120520	NM_000902	3q21-q27
			calpain, large polypeptide L3/CAPN3	114240	NM_000070	5q15.1-q21.1
			leucyl/cystinyl	151300	NM_005575	*****
			carboxypeptidase N polypeptide 1/CPNI	603103	NM_001308	chr. 10

4czf01.xls

Adrenocorticotrophic Hormone	Corticotropin releasing hormone receptor 2/CRHR2	602034	NM_001883	7p21-p15
	Corticotropin releasing hormone-binding protein/CRHBP	122559	NM_001882	5q11.2-q13.3
	proopiomelanocortin/POMC	176830	NM_000939	2p23.3
ACTH	melanocortin 2 receptor/ACTH receptor/MC2R	202200	NM_000529	18p11.2
	thyrotropin releasing hormone/TRH	275120	NM_007117	3p
	thyrotropin releasing hormone receptor/G protein coupled/TRHR	188545	NM_003301	8q23
TSH	cAMP responsive element binding protein 1/CREB1	123810	NM_004379	2q32.3-q34
	chorionic gonadotropin alpha chain/TSHA/CGA	118850	NM_000735	6q21.1-q23
	thyroid stimulating hormone beta chain/TSHB	188540	NM_000549	1p13
Thyroid Hormone	thyroid stimulating hormone receptor/TSHR	603372	NM_000369	14q31
	solute carrier family 5 (sodium iodide symporter), member 5/SLC5A5	601843	NM_000453	19p13.2-p12
	thyroid peroxidase (nuclear gene encoding mitochondrial protein)/TPO	274500	NM_000547	2p25
	thyroglobulin/TG	188450	NM_003235	8q24.2-q24.3
	thyroxine-binding globulin/TBG	314200	NM_000354	Xq22.2
	transthyretin (prealbumin, amyloidosis type I)/TTR	176300	NM_000371	18q11.2-q12.1

Peptide Hormones Control of Metabolism	Thyroid Hormone Synthesis	deiodinase, iodothyronine, type I/DIO1	147892	NM_00079 2	1p33-p32
		deiodinase, iodothyronine, type II/DIO2	601413	NM_00079 3	14q24.2- q24.3
		thyroid hormone receptor, alpha (avian erythroblastic leukemia viral (v-erb-a) oncogene homolog)/THRA	190120	NM_00325 0	17q11.2
		thyroid hormone receptor, alpha (avian erythroblastic leukemia viral (v-erb-a) oncogene homolog 2)/THRB	190160	S57224	3p24.3
		thyroid hormone receptor coactivating protein/SMAP	601836	NM_00669 6	*****
		silencing mediator for retinoid and thyroid hormone receptors/SMRT	600848	NM_006312	*****
		retinoic and thyroid hormone receptor associated corepressor 1/TRAC1/NCOR1	600849	NM_006311	*****
		deiodinase, iodothyronine, type III/DIO3	601038	NM_00136 2	14q32
	GNRH (common to all gonadotropin s except CGH)	gonadotropin releasing hormone 1/LHRH/GNRH1	152760	NM_000825	8p21-p11.2
		gonadotropin releasing hormone 2/LHRH/GNRH2	602352	NM_001501	20p13
		gonadotropin releasing hormone receptor/G protein- coupled/LHRHR/GNRHR	138850	NM_000406	4q21.2
		prolactin/PRL	176760	NM_000948	6p22.2-p21.3
	Prolactin	prolactin receptor/PRLR	176761	NM_000949	5p13-p12

Leuteinizing Hormone	cAMP responsive element binding protein 1/CREB1	123810	NM_004379	2q32.3-q34
	glycoprotein hormones, alpha polypeptide/CGAa	118850	NM_000735	6q21.1-q23
	leuteinizing hormone beta polypeptide/LHB	152780	NM_000894	19q13.32
	leuteinizing hormone/choriogonadotropin	152790	NM_000233	2p21
Follicle Stimulating Hormone	glycoprotein hormones, alpha polypeptide/CGAa	118850	NM_000735	6q21.1-q23
	follicle stimulating hormone-inhibin, beta A (activin A, activin AB alpha polypeptide)/INHBA	136530	AH002701	11p13
	activin A receptor, type I/ACVR1	147290	NM_002192	7p15-p13
	activin A receptor, type IB/ACVR1B	102576	NM_001105	2q23-q24
	activin A receptor type II-like I/ACVRL1	601300	NM_004302	12q13
	activin typeII A receptor/ACVR2	601284	NM_000020	12q11-q14
	activin A receptor, type IIB/ACVR2B	102581	NM_001616	*****
	alpha-inhibin/INHBA	602730	NM_001106	3p22-p21.3
	beta-B inhibin/beta C inhibin/INHBC	147380	NM_001106	2q33-q36
	folliculin/FST	601233	NM_005538	12q13.1
	follicle stimulating hormone receptor/FSHR	136470	NM_006350	5p14
	FSH primary response (LRPR1, rat) homolog 1/FSHPRH1	136435	NM_000145	2p21-p16
	homolog 1/FSHPRH1	300065	NM_006733	Xq22
Gonadotropin Hormones	glycoprotein hormones, alpha polypeptide/CGAa	118850	NM_000735	6q21.1-q23

Chorionic Gonadotropin	chorionic gonadotropin, beta polypeptide/CGB	118860	NM_000737	19q13.32
	luteinizing hormone/choriogonadotropin	152790	NM_000233	2p21
Anabolism	3-hyd oxy-3-methylglutaryl-Coenzyme A synthase 1	142940	NM_002130	5p14-p13
	HMGCoA reductase/HMGCR	142910	NM_000859	5q13.3-q14
	squalene synthetase/arnesyl-diphosphate farnesyltransferase	184420	NM_004462	8p23.1-p22
	steroid-5-alpha-reductase, alpha polypeptide 1 (3-oxo-5 alpha-steroid delta 4-dehydrogenase alpha 1)/SRD5A1	184753	NM_001047	5p15
	steroid-5-alpha-reductase, alpha polypeptide 2 (3-oxo-5 alpha-steroid delta 4-dehydrogenase alpha 2)/SRD5A2	264600	NM_000348	2p23
	steroidogenic acute regulatory protein/STAR	600617	NM_000349	8p11.2
	cytochrome P450, subfamily XIA (cholesterol side chain cleavage)/CYP11A	118485	NM_000781	15q23-q24
	ferredoxin 1/FDX1	103260	NM_004109	11q22
	cytochrome P450, subfamily XVII (steroid 17-alpha-hydroxylase), adrenal hyperplasia/CYP17	202110	NM_000102	10q24.3
General Steroid Hormone Metabolism				

(additional genes in Toxicology)	hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 1/HSD3B1	109715	NM_00086 2	1p13.1
	hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 2/HSD3B2	201810	NM_00019 8	1p13.1
Catabolism	dehydroepiandrosterone (DHEA)- preferring sulfotransferase, family 2A, member 1/SULT2A1	125263	NM_00316 7	19q13.3
	estrogen-preferring	600043	NM_005420	4q13.1
	UDP glycosyltransferase 1/UGT1	191740	NM_00107 2	Chr. 12
	UDP glycosyltransferase family 2, member B4/UGT2B4	600067	NM_00107 3	4q13
	UDP glycosyltransferase family 2, member B7/UGT2B7	600068	NM_00107 4	1q14
	UDP glycosyltransferase 2 family, polypeptide B11/UGT2B11	603064	NM_00107 3	*****
	UDP glycosyltransferase family 2, member B15/UGT2B15	600069	NM_00107 6	4q13
	UDP glycosyltransferase family 2, member B17/UGT2B17	601903	NM_00107 7	1q14
	hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 1/HSD3B1	109715	NM_00086 2	1p13.1
	hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 2/HSD3B2	201810	NM_00019 8	1p13.1
Synthesis				

Progestins	Receptors	progesterone receptor/PGR	264080	NM_000926	11q22
		heat shock 90-kD protein 1, alpha subunit/HSPCA	140571	*****	1q21.2-q22
		heat shock 90-kD protein 1, beta subunit/HSPCB	140572	J04988	6p12
		FK506-binding protein 5/FKBP5	602623	NM_004117	*****
Steroid Hormones	Synthesis	cytochrome P450, subfamily XIX (androgen aromatase)/CYP19	107910	NM_000103	15q21.1
		estrogen receptor 1/ESR1	133430	NM_000125	6q25.1
	Receptors	estrogen receptor 2/ESR2	601663	X99101	14q
		estrogen-related receptor	601998	NM_004451	11q12
	Catabolism	estrogen-related receptor beta/ESRRB	602167	NM_004452	14q24.3
		estrogen-preferring	600043	NM_005420	4q13.1
Androgens	Synthesis	steroid-5-alpha-reductase, alpha polypeptide 1 (3-oxo-5 alpha-steroid delta 4-dehydrogenase alpha 1)/SRD5A1	184753	NM_001047	5p15
		hydroxysteroid (17-beta) dehydrogenase 3/HSD17B3	264300	NM_000197	9q22
		cytochrome P450, subfamily XIA (cholesterol side chain cleavage)/CYP11A	118485	NM_0000781	15q23-q24
		steroid 5-alpha-reductase 2/SRD5A2	264600	NM_000348	2p23
	Receptor	androgen receptor (dihydrotestosterone receptor)/AR	313700	NM_000044	Xq11-q12
		UDP glycosyltransferase 2 family, polypeptide B17/UGT2B17	601903	NM_001077	4q13
	Catabolism				

Glucocorticoids (cortisol, corticosterone)	Synthesis	cytochrome P450, subfamily XXI (steroid 21-hydroxylase)/CYP21	201910	X58902	6p21.3
		cytochrome P450, subfamily XIB (steroid 18-beta-hydroxylase), polypeptide 2/CYP11B2	124080	NM_000498	8q21
		cytochrome P450, subfamily XIB (steroid 11-beta-hydroxylase), polypeptide 1/CYP11B1	202010	NM_000497	8q21
		glucocorticoid receptor/GRL	138040	NM_000176	5q31
		heat shock 70kD protein 1/HSPA1A	140550	NM_005345	6p21.3
		heat shock 70kD protein-like 1/HSPA1L	140559	NM_005527	6p21.3
		heat shock 70kD protein 1/HSPA1B	603012	NM_005346	6p21.3
	Receptor and Cofactors	heat shock 90-kD protein 1, alpha subunit/HSPCA	140571	*****	1q21.2-q22
		heat shock 90-kD protein 1, beta subunit/HSPCB	140572	J04988	6p12
		FK506-binding protein 4 (59kD)/FKBP4	600611	NM_002014	*****
		mineralocorticoid receptor/MCR/nuclear receptor subfamily 3, group C, member	600983	NM_000901	4q31.1
	Transport and Catabolism	corticosteroid binding globulin precursor/CBG	122500	NM_001756	14q32.1
		hydroxy-D-5-steroid dehydrogenase, 3 b- and steroid D-isomerase 2/HSD3B2	201810	NM_000198	1p13.1
		cytochrome P450, subfamily XIB, polypeptide 2 (steroid 11-b- hydroxylase)/CYP11B2	124080	NM_000498	8q21

Mineralocorticosteroids (aldosterone, deoxycorticosterone)	Synthesis	sodium channel, nonvoltage-gated 1 alpha/SCNN1A	600228	NM_001038	12p13
		sodium channel, nonvoltage-gated 1, beta (Liddle syndrome)/SCNN1B	600760	NM_000336	16p13-p12
		sodium channel, nonvoltage-gated 1, gamma/SCNN1G	600761	NM_001039	16p13-p12
		mineralocorticoid receptor/MCR/nuclear receptor subfamily 3, group C, member	600983	NM_000901	4q31.1
Mediators of Steroid Response	Receptor	nuclear receptor coactivator 2/GRIP1	601993	NM_006540	*****
		oxysterol binding protein/OSBP	167040	NM_002556	11q12-q13
		sterol regulatory element binding transcription factor 1/SREBF1	184756	NM_004176	17p11.2
		sterol regulatory element binding transcription factor 2/SREBF2	600481	NM_004599	22q13
		steroid receptor coactivator 1/SRC1	602691	NM_003743	2p23
		steroid receptor RNA activator/SRA	603819	AF092038	Chr. 5
Serotonin	Receptors	5-hydroxytryptamine (serotonin) receptor 2C (G protein-coupled)/HTR2C	312861	NM_000868	Xq24
		dopamine receptor D1/DRD1	126449	NM_000794	5q35.1
Dopamine	Receptors	dopamine receptor D2/DRD2	126450	NM_000795	11q23
Norepinephrine	Receptors	adrenergic, beta-2-, receptor, surface/ADRB2	109690	NM_000024	5q32-q34
		adrenergic, beta-3-, receptor/ADRB3	109691	NM_000025	8p12-p11.2
		Neuropeptide Y/NPY	162640	NM_000905	7p15.1
Neuropeptides	Biosynthesis	Neuropeptide Y receptor Y1/NPY1R	162641	NM_000909	4q31.3-q32
		Neuropeptide Y receptor Y2/NPY2R	162642	NM_000910	4q31

Neuropeptide Y (NPY)	Receptors	Neuropeptide Y receptor Y3/chemokine receptor	162643	X71635	2q21
		Neuropeptide Y receptor Y5/NPY5R	602001	NM_006174	4q31-q32
		Neuropeptide Y receptor Y6/NPY6R	601770	NM_006173	5q31
	Biosynthesis	preprogalanin/GAL1	137035	L11144	1q13.3-q13.5
Galanin	Receptor	galanin receptor 1 (brain)/GALR1	600377	NM_001480	18q23
		galanin receptor 2/GALR2	603691	NM_003857	17q25.3
		galanin receptor 3 (brain)/GALR3	603692	NM_003614	2q12.2-q13.1
		pro-melanin-concentrating hormone/PMCH	176795	NM_002674	12q23-q24
Pro-Melanin Concentrating Hormone	Biosynthesis	pro-melanin-concentrating hormone-like 1/PMCHL1	176793	*****	5p14
		pro-melanin-concentrating hormone-like 2/PMCHL2	176794	AF064698	5q12-q13
		melanin-concentrating hormone receptor/MCHR/G protein-coupled receptor 24/GPR24	601751	NM_005297	22q13.3
		proopiomelanocortin/POMC	176830	NM_000939	2p23.3
Melanocortin	Receptors	melanocortin 1 receptor (alpha melanocyte stimulating hormone receptor)/MC1R	155555	NM_002386	16q24.3
		melanocortin 4 receptor/MC4R	155541	NM_005912	18q22
		melanocortin 5 receptor/MC5R	600042	NM_005913	18p11.2
	Regulation	agouti (mouse)-signaling protein/ASIP	600201	NM_001672	20q11.2
		cAMP responsive element binding protein 1/CREB1	123810	NM_004379	2q32.3-q34

Peptide Hormonal Regulation of Appetite	Opioids	Biosynthesis	preproenkephalin B/prodynorphin/PDYN	131340	NM_006211	20pter-p12.2.1
		Receptors	preproenkephalin A/proenkephalin/PENK	131330	NM_006211	8q23-q24
	Cholecystokinin (CCK)	Biosynthesis	opioid receptor, kappa 1/OPRK1	165196	NM_000912	8q11.2
		Receptors	Cholecystokinin/CCK	118440	NM_000729	3pter-p21
		Biosynthesis	Cholecystokinin A receptor/CCKAR	118444	NM_000730	4p15.2-p15.1
		Receptors	Cholecystokinin B receptor/CCKBR	118445	NM_000731	1p15.5-p15.4
		Biosynthesis	corticotropin releasing hormone/CRH	122560	NM_000756	8q13
		Receptors	urocortin/UCN	600945	NM_003353	Chr.2
	Adrenocorticotropic Hormone	Biosynthesis	urocortin 2/UCN2	604097	AF104118	*****
		Receptors	Corticotropin releasing hormone receptor 1/CRHR1	122561	U16273	17q12-q22
		Receptors	Corticotropin releasing hormone receptor 2/CRHR2	602034	NM_001883	7p21-p15
		Signalling	Corticotropin releasing hormone-binding protein/CRHBP	122559	NM_001882	5q11.2-q13.3
	PACAP	Biosynthesis	adenylate cyclase activating polypeptide 1 (pituitary)/ADCYAP1	102980	NM_001117	18p11
		Receptor	adenylate cyclase activating polypeptide 1 (pituitary) receptor type I/ADCYAP1R1	102981	NM_001118	7p14
	Enterostatin	Biosynthesis	enterostatin/colipase, pancreatic/CLPS	120105	NM_001832	6pter-p21.1
	Insulin	Biosynthesis	insulin/INS	176730	NM_000207	11p15.5
		Receptor	insulin receptor/INSR	147670	NM_000208	19p13.2
		Biosynthesis	leptin/LEP	164160	NM_000230	7q31.3
		Receptor	peroxisome proliferative activated receptor, gamma/PPARG	601487	NM_005037	3p25

Leptin	Receptor	leptin receptor/LEPR	601007	NM_002303	1p31
	Signalling	signal transducer and activator of transcription 3/STAT3	102582	NM_003150	17q21
		signal transducer and activator of transcription 5A/STAT5A	601511	NM_003152	17q11.2
		signal transducer and activator of transcription 6, interleukin-4 induced/STAT6	601512	NM_003153	12q13
Thyroid Hormone	Biosynthesis	thyrotropin releasing hormone/TRH	275120	NM_007117	3p
	Receptors	thyrotropin releasing hormone receptor/G protein coupled/TRHR	188545	NM_003301	8q23
Glucagon	Biosynthesis	paired box gene 6/PAX6	106210	NM_000280	11p13
		preproglucagon/GCG	138030	NM_002054	2q36-q37
	Receptor	glucagon receptor/GCGR	138033	NM_000160	17q25
		glucagon-like peptide 1	138032	NM_002062	6p21
		glucagon-like peptide 2	603659	NM_004246	17p13.3
Glucagon-Like Polypeptides	Biosynthesis	paired box gene 6/PAX6	106210	NM_000280	11p13
		preproglucagon/GCG	138030	NM_002054	2q36-q37
	Receptors	glucagon-like peptide 1	138032	NM_002062	6p21
		glucagon-like peptide-2 receptor precursor/GLP2R	603659	AF105367	17p13.3
		somatostatin transcription factor 1/STF1/homeodomain transcription factor/insulin promoter factor 1/IPF1	600733	NM_000209	13q12.1
		paired box gene 6/PAX6	106210	NM_000280	11p13
		paired box gene 4/PAX4	167413	NM_006193	7q32

Control of Metabolism	Insulin	Biosynthesis			
		Homo sapiens paired box gene	167415	NM_003466	2q12-q14
		insulin/INS	176730	NM_000207	11p15.5
		neurogenic differentiation	601724	NM_002500	2q32
		cAMP responsive element binding protein 1/CREB1	123810	NM_004379	2q32.3-q34
		lim homeobox transcription factor 1, alpha/LIMX1A	600298	*****	1q22-q23
		caudal type homeo box transcription factor 2/CDX2	600297	NM_001265	13q12.3
		purine-rich element binding protein A/PURA	600473	NM_005859	5q31
		ATP-binding cassette, sub-family C, member 8/ABCC8/sulfonylurea receptor (hyperinsulinemia)/SUR1	600509	NM_000352	11p15.1
		ATP-binding cassette, sub-family C (C	601439	NM_005691	12p12.1
Receptor	Insulin	beta-cell inward rectifier subunit/BIR/potassium inwardly-rectifying channel, subfamily J, member 11/KCNJ11	600937	D50582	11p15.1
		carboxypeptidase E/CPE	114855	NM_001873	Chr.4
		insulin receptor/INSR	147670	NM_000208	19p13.2
		insulin receptor substrate 1/IRS1	147545	NM_0055544	2q36
		insulin receptor substrate 2/IRS2	600797	NM_003749	13q34
		insulin receptor substrate 4/IRS4	603510	NM_003604	*****
		growth factor receptor-bound protein 10/GRB10	601523	NM_005311	7p12-p11.2

		growth factor receptor-bound protein 2/GRB2	108355	NM_002086	17q24-q25
	Signaling	amylin/diabetes-associated peptide/DAP/islet amyloid polypeptide/IAPP	147940	NM_000415	12p12.3-p12.1
	Metabolism	insulin-degrading enzyme/IDE	146680	NM_004969	10q23-q25
		uncoupling protein 1 (mitochondrial, proton carrier)/UCP1	113730	X51953	4q31
	Uncoupling Proteins	uncoupling protein 2 (mitochondrial, proton carrier)/UCP2	601693	AF019409	11q13
		uncoupling protein 3 (mitochondrial, proton carrier)/UCP3	602044	NM_003356	11q13
		uncoupling protein 4 (mitochondrial, proton carrier)/UCP4	*****	NM_004277	*****
		somatostatin transcription factor 1/STF1/homeodomain transcription factor/insulin promoter factor 1/IPF1	600733	NM_000209	13q12.1
	Biosynthesis	paired box gene 6/PAX6	106210	NM_000280	11p13
		cAMP responsive element binding protein 1/CREB1	123810	NM_004379	2q32.3-q34
		somatostatin/SST	182450	NM_001048	3q28
	Somatostatin	preprocartistatin/CORT	602784	NM_001302	1p36
		Somatostatin receptor 1/G protein-coupled/SSSTR1	182451	NM_001049	14q13
		Somatostatin receptor 2/SSSTR2	182452	NM_001050	17q24
		Somatostatin receptor 3/adenyl cyclase coupled/SSSTR3	182453	NM_001051	22q13.1
		Somatostatin receptor 4/SSSTR4	182454	NM_001052	20p11.2
	Receptors				

	Somatostatin receptor 5/SSSTR5	182455	NM_001053	16p13.3
GHRH	growth hormone releasing hormone/GHRH	139190	AH002712	20q11.2
	growth hormone releasing hormone receptor/G protein-coupled/GHRHR	139191	NM_000823	7p15-p14
Growth Hormone	growth hormone 1/somatotropin/GH1	139250	NM_000515	17q22-q24
	growth hormone receptor/GHR	600946	NM_000163	5p13-p12
Biosynthesis	insulin-like growth factor 1 (somatomedin C)/IGF1	147440	M27544	12q22-q24.1
	insulin-like growth factor 2 (somatomedin A)/IGF2	147470	NM_000612	11p15.5
	insulin-like growth factor 1 receptor precursor/IGF1R	147370	NM_000875	15q25-q26
Receptor	insulin-like growth factor 2 receptor/IGF2R	147280	NM_000876	6q26
	insulin-like growth factor binding protein/IGFBP1	146730	NM_000596	7p14-p12
Insulin-Like Growth Factor	insulin-like growth factor binding protein/IGFBP2	146731	M35410	2q33-q34
	insulin-like growth factor binding protein/IGFBP3	146732	NM_000598	7p14-p12
	insulin-like growth factor binding protein/IGFBP4	146733	Y12508	17q12-q21
	insulin-like growth factor binding protein/IGFBP5	146734	AF055033	2q33-q36
	insulin-like growth factor binding protein/IGFBP6	146735	M69054	12q13
	insulin-like growth factor binding protein/IGFBP7	602867	NM_001553	4q12
	connective tissue growth factor/CTGF	121009	NM_001901	6q23.1
	insulin-like growth factor binding protein/IGFBP8	602369	NM_001554	1p22.3
Catabolism	insulin-like growth factor binding protein/IGFBP9	601489	NM_004970	Chr. 16
	protease, serine, 11 (IGF binding)/PRSS11	602194	NM_002775	0q25.3-q26.2
	heparin-binding growth factor 1/FGF1	131220	NM_000800	5q31
	basic fibroblast growth factor/FGF2	134920	NM_002006	4q25-q27

Fibroblast Growth Factor	fibroblast growth factor 3/FGF3	164950	NM_005247	11q13
	HST oncogene/fibroblast growth factor 4/FGF4	164980	NM_002008	11q13
	fibroblast growth factor-related protein/FGF5	165190	NM_004464	4q21
	fibroblast growth factor 6/FGF6	134921	X57075	12p13
	keratinocyte growth factor/fibroblast growth factor 7/FGF7	148180	NM_002009	15q15-q21.1
	fibroblast growth factor 8 (androgen-induced)/FGF8	600483	NM_006119	10q24
	fibroblast growth factor 9 (glia-activating factor)/FGF9	600921	NM_002010	13q11-q12
	fibroblast growth factor 10/FGF10	602115	NM_004465	5p13-p12
	fibroblast growth factor 11/FGF11	601514	NM_004112	17q21
	fibroblast growth factor 12/FGF12	601513	*****	3q28
	fibroblast growth factor 13/FGF13	300070	NM_004114	Xq26.3
	fibroblast growth factor 14/FGF14	601515	NM_004115	13q34
	fibroblast growth factor 16/FGF16	603724	NM_003868	*****
	fibroblast growth factor 17/FGF17	603725	NM_003867	8p21
	fibroblast growth factor 18/FGF18	603726	NM_003862	*****
	fibroblast growth factor 19/FGF19	603891	NM_005117	*****
	fibroblast growth factor receptor 1/FGFR1	136350	*****	8p11.2-p11.1
Receptors	fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crouzon syndrome, Pfeiffer syndrome, Jackson-Weiss syndrome)/FGFR2	176943	NM_000141	10q26

General Growth Control		fibroblast growth factor receptor 3 (achondroplasia, thanatophoric dwarfism)/FGFR3	134934	NM_00524 7	4p16.3	
		fibroblast growth factor receptor 4/FGFR4	134935	NM_00201 1	5q35.1-qter	
	Signaling	FGFR1 oncogene partner/FOP	*****	NM_007045	*****	
		suc1-associated neurotrophic factor target 1 (FGFR signalling adaptor)/SNT1	*****	NM_006654	*****	
		suc1-associated neurotrophic factor target 2 (FGFR signalling adaptor)/SNT2	*****	NM_006653	*****	
		sonic hedgehog (Drosophila) homolog/SHH	600725	NM_000193	7q36	
	Sonic Hedgehog	Indian hedgehog (Drosophila) homolog/IHH	600726	L38517	2q33-q35	
		Receptors	patched (Drosophila) homolog/PTCH	601309	NM_000264	9q22.3
	Nerve Growth Factor	Biosynthesis	nerve growth factor, alpha subunit/NGFA	162020	*****	*****
			nerve growth factor, beta	162030	*****	1p13.1
nerve growth factor, gamma subunit/NGFG			162040	*****	19q13.3	
Receptors		nerve growth factor receptor (TNFR superfamily, member 16)/NGFR	162010	NM_002507	17q21-q22	
Neurotrophins	Biosynthesis	neurotrophin 3/NTF3	162660	NM_002527	12p13	
		neurotrophin 5 (neurotrophin)	162662	NM_006179	19q13.3	
		neurotrophin 6, alpha/NTF6A	604021	NM_004149	19q13.3	
		neurotrophin 6, beta/NTF6B	604022	NM_004150	19q13.3	
		neurotrophin 6, gamma/NTF6G	604023	NM_004151	19q13.3	

neurotrophic tyrosine kinase receptor type 1/NTRK1	191315	Y09033	1q21-q22
	600456	NM_006180	9q22.1
	191316	NM_002530	15q25
	171833	M61906	5q13
neurotrophic tyrosine kinase receptor type 2/NTRK2	603157	NM_005027	19q13.2-q13.4
	*****	NM_003629	*****
	171834	NM_006218	3q26.3
	602925	NM_006219	*****
neurotrophic tyrosine kinase receptor type 3/NTRK3	602839	NM_005026	1p36.2
	601232	NM_002649	*****
	182530	NM_005633	2p22-p21
	190020	NM_005343	11p15.5
phosphatidylinositol 3-kinase, regulatory subunit, polypeptide 1 (p85, alpha)/PIK3R1	190070	NM_004985	12p12.1
phosphatidylinositol 3-kinase, regulatory subunit, polypeptide 2 (p85, beta)/PIK3R2			
phosphatidylinositol 3-kinase, regulatory subunit, polypeptide 3 (p55, gamma)/PIK3R3			
phosphoinositide-3-kinase, catalytic, alpha polypeptide/PIK3CA			
phosphoinositide-3-kinase, catalytic, beta polypeptide/PIK3CB			
phosphatidylinositol 3-kinase, catalytic, delta polypeptide/PIK3CD			
phosphatidylinositol 3-kinase, catalytic, gamma polypeptide/PIK3CG			
son of sevenless (Drosophila) homolog 1/SOS1			
v-Ha-ras Harvey rat sarcoma viral oncogene homolog/HRAS			
v-Ki-ras2 Kirsten rat sarcoma 2 viral oncogene homolog/KRAS2			

Mediators	neuroblastoma RAS viral (v-ras) oncogene homolog/NRAS	164790	NM_002524	1p13.2
	Ras-related associated with diabetes/RRAD	179503	NM_004165	16q22
	v-raf-1 murine leukemia viral oncogene homolog 1/RAF1	164760	NM_002880	3p25
Hormone Signalling	mitogen activated protein kinase PRKM1/MAPK1	176948	NM_002745	22q11.2
	mitogen activated protein kinase PRKM3/MAPK3	601795	X60188	16p11.2
	mitogen activated protein kinase PRKM4/MAPK4	176949	NM_002747	18q12-q21
	mitogen activated protein kinase PRKM6/MAPK6	602904	NM_002748	*****
	mitogen activated protein kinase PRKM7/MAPK7	602521	NM_002749	17p11.2
	mitogen activated protein kinase JNK1/PRKM8/MAPK8	601158	L26318	*****
	mitogen activated protein kinase JNK2/PRKM9/MAPK9	602896	U09759	5q35
	mitogen activated protein kinase JNK3/PRKM10/MAPK10	602897	U35003	*****
	mitogen activated protein kinase PRKM11/MAPK11	602898	AF031135	*****
	mitogen activated protein kinase SAPK3/MAPK12	602399	NM_002969	22q13.3
	mitogen activated protein kinase PRKM13/MAPK13	602899	NM_002754	*****
	mitogen activated protein kinase SAPK2A/MAPK14	600289	NM_001315	6p21.3-p21.2
Protein Kinases				

Protein Phosphatases	protein tyrosine phosphatase, non-receptor type 1/PTPN1	176885	NM_002827	20q13.1-q13.2
	protein tyrosine phosphatase, receptor type, F/PTPRF	179590	NM_002840	1p32
	protein phosphatase 1, catalytic subunit, alpha isoform/PPP1CA	176875	NM_002708	11q13
	phogrin/IAR/receptor-like protein-tyrosine phosphatase precursor/IAR	601698	AF007555	7q36
	protein tyrosine phosphatase, receptor type, N/PTPRN	601773	NM_002846	2q35-q36.1
	protein phosphatase 1, regulatory (inhibitor) subunit 2/PPP1R2	601792	NM_006241	3q29
Other	insulin induced gene 1/INSIG1	602055	NM_005542	7q36
Gluconeogenesis	pyruvate carboxylase/PC	266150	NM_000920	11q13.4-q13.5
	phosphoenolpyruvate carboxykinase 1 (soluble)/PEPCK1/PCCK1	261680	NM_002591	20q13.31
	phosphoenolpyruvate carboxykinase 2 (mitochondrial)/PEPCK2/PCCK2	261650	NM_004563	*****
	aminomethyltransferase (glycine cleavage system protein T)/AMT	238310	NM_000481	3p21.2-p21.1
	glycine decarboxylase			
	(decarboxylating; glycine decarboxylase, glycine cleavage system protein L)/PDCD	238300	NM_000170	9p22
Glycogen Storage	glycogenin/GYG	603942	NM_004130	3q24-q25.1
	glycogenin 2/GYG2	300198	NM_003918	Xp22.3

Storage	glycogen synthase 1 (muscle)/GYS1	138570	NM_002103	19q13.3
	glycogen synthase 1 (liver)/GYS2	138571	AJ003087	12p12.2
Regulation of Glycogen Metabolism	phosphorylase kinase, alpha 1 (muscle), muscle	311870	NM_002637	Xq13
	phosphorylase kinase, alpha 2 (liver), glycogen storage disease IX/PHKA2	306000	NM_000292	Xp22.2-p22.1
	phosphorylase kinase, beta/PHKB	172490	NM_000293	16q12-q13.1
	phosphorylase kinase, gamma 2 (testis)	172471	NM_000294	6p12.1-p11.2
	protein phosphatase 1, regulatory (inhibitor) subunit 3 (glycogen and sarcoplasmic reticulum binding subunit, skeletal muscle)/PPP1R3	600917	NM_002711	*****
	albumin proximal factor/transcription factor 1/TCF1/hepatic nuclear factor/HNF1	142410	NM_000545	12q24.2
	transcription factor 2/TCF2/hepatic nuclear factor 2/HNF2	189907	NM_006481	17cen-q21.3
	hepatocyte nuclear factor 3, alpha/HNF3A	602294	NM_004496	14q12-q13
	hepatocyte nuclear factor-3 beta/HNF3B	600288	AF176110	20p11
	hepatocyte nuclear factor 3, gamma/HNF3G	602295	NM_004497	19q13.2-q13.4
	hepatocyte nuclear factor 4, alpha/HNF4A	600281	NM_000457	20q12-q13.1
	hepatocyte nuclear factor 6/HNF6	604164	AH007195	15q21.1-q21.2

Metabolism

Carbohydrate Metabolism and Storage

	amylo-1,6-glucosidase, 4-alpha-glucanotransferase (glycogen debranching enzyme, glycogen storage disease type III)/AGL	232400	NM_000642	1p21
Glycolysis	hexokinase 2, nuclear gene encoding mitochondrial protein/HK2	601125	NM_000189	2p12
	glucokinase (hexokinase 4, maturity onset diabetes of the young 2) nuclear gene encoding mitochondrial protein/GCK	138079	NM_000162	7p15-p13
	phosphofructokinase, muscle/PFKM	232800	NM_000289	12q13.3
	pyruvate kinase, muscle/PKM2	179050	NM_002654	15q22
	pyruvate kinase, liver/PKL	*****	D13243	*****
	pyruvate dehydrogenase (lipoamide) alpha 1/PDHA1	312170	NM_000284	Xp22.2-p22.1
	pyruvate dehydrogenase (lipoamide) al	179061	NM_005390	4q22-q23
	pyruvate dehydrogenase (lipoamide) be	179060	NM_000925	3p13-q23
	pyruvate dehydrogenase dihydrolipoam	246900	NM_000108	7q31-q32
	pyruvate dehydrogenase lipoyl-contain	245349	NM_003477	11p13
	beta-galactosidase/GLB1	230500	M22590	3p21.33
	cathepsin A/CSTA/protective protein for beta-galactosidase (galactosialidosis)/PPGB	256540	NM_000308	20q13.1

Glycolytic (and Other) Protein Maturation and Targeting	Lysosomal Targeting of Glycolytic Enzymes	amyloid precursor protein secretase/cathepsin B/CTSB	116810	NM_001908	8p22
		dipeptidyl-peptidase I/DPP1/cathepsin C/CTSC	602365	NM_001814	1q14.1-q14.2
		cathepsin D (lysosomal aspartyl/ protease)/CTSD	116840	NM_001909	11p15.5
		cathepsin E/CTSE	116890	NM_001910	1q31
		cathepsin F/CTSF	603539	AF132894	11q13
		cathepsin G/CTSG	116830	NM_001911	14q11.2
		granzyme H/GZMH/cathepsin G-like 2/CSTGL2	116831		14q11.2
		cathepsin H/CTSH	116820	NM_004390	15q24-q25
		cathepsin K (pseudodysostosis)/CTSK	601105	NM_000396	1q21
		cathepsin L/CTSL	116880	NM_001912	9q21-q22
		cathepsin L2/CTSL2	*****	NM_001333	*****
		cathepsin O/CTSO	600550	NM_001334	4q31-q32
		cathepsin S/CTSS	116845	NM_004079	1q21
		cathepsin U/CTSU	*****	AF070448	*****
		cathepsin V/CTSV	*****	AB001928	*****
		cathepsin W/CTSW	602364	NM_001335	11q13.1
		cathepsin X precursor/CSTX	*****	AF073890	*****
		cathepsin Z/CTSZ	603169	NM_001336	20q13
		mannosyltransferase polypeptide 1	603503	NM_003859	*****
		mannosyltransferase polypeptide 2	603564	NM_003863	*****
		dolichyl-phosphate (UDP-N- acetylglucosamine) N- acetylglucosaminophosphotransferase 1 (GlcNAc-1-P transferase)/DPAGT1	191350	NM_001382	11q23.3

Protein Glycosylation (enzymatic and non- enzymatic)	aldose reductase/aldo-keto reductase family 1, member A1 (aldehyde reductase)/AKR1A1	103880	NM_00606 6	7q35
	sorbitol dehydrogenase/SORD	182500	NM_00310 4	15q15.3
Sugar and Transition Metal Metabolism	glutamine-fructose-6-phosphate transaminase 1/GFPT1	138292	NM_00205 6	2p13
	glutamine-fructose-6-phosphate transaminase 2/GFPT2	603865	NM_00511 0	5q34-q35
	receptor for advanced glycation end products/RAGE/AGER	600214	AJ133822	6p21.3
	glutamate-cysteine ligase (gamma- glutamylcysteine synthetase), catalytic (72.8kD)/GLCLC	230450	NM_00149 8	6p12
	glutathione synthetase/GSS	601002	NM_00017 8	20q11.2
	ATP-binding cassette 7 (iron transporter)/ABCB7	300135	NM_00429 9	Xq13.1- q13.3
	transferrin/TF	190000	NM_00106 3	3q21
	hepatocyte growth factor/HGF	142409	G_HUMHG	7q21.1
	hepatocyte growth factor receptor/oncogene MET/MET/HGFR	164860	NM_00024 5	7q31
	vascular endothelial growth factor/VEGFA	192240	NM_00337 6	6p12
	vascular endothelial growth factor/VEGFB	601398	NM_00337 7	11q13
	vascular endothelial growth factor/VEGFC	601528	NM_00542 9	*****
	VEGF receptor/VEGFR	191306	AF063657	4q12

Neovascularization	Vascular Growth Factors and Inhibitors	growth hormone/GHI	139250	NM_000515	17q22-q24
		growth hormone receptor/GHR	600946	NM_000163	5p13-p12
		pigment epithelium-derived	172860	NM_002615	17p13.3
		angiostatin/plasminogen/PLG	173350	NM_000301	6q26
		endostatin/type XVIII collagen/COL18A1	120328	AF018081	21q22.3
		endothelin 1/EDN1	131240	NM_001955	6p24-p23
		endothelin 2/EDN2	131241	NM_001956	1p34
		endothelin 3/EDN3	131242	NM_000114	20q13.2-q13.3
		endothelin A receptor isoform delta			
		3/EDNRA	131243	AF014826	Chr.4
		endothelin receptor type B/EDNRB	131244	NM_000115	13q22
		protein kinase C beta/PRKCB	176970	X06318	16p11.2
		transforming growth factor, beta-1/TGFB1	190180	M60315	9q13.1-q13.3
		transforming growth factor, beta-2/TGFB2	190220	NM_003238	1q41
		transforming growth factor, beta-3/TGFB3	190230	NM_003239	14q24
		transforming growth factor, beta receptor I (activin A receptor type II-like kinase, 53kD)/TGFBRI	190181	NM_004612	9q33-q34
		transforming growth factor, beta receptor II (70-80kD)/TGFB2	190182	NM_003242	3p22
		transforming growth factor, beta receptor III (betaglycan, 200kD)/TGFB3	600742	NM_003243	1p33-p32
		decorin/DCN	125255	NM_001920	12q23
		Munc13	*****	AF020202	*****

Hypertension (hypoxia, vascular endothelium thickening, and hypertension)	Ion Pump	transient receptor potential channel 3 (diacylglycerol-activated non-selective cation channel)/TRPC3	602345	NM_003305	*****
		transient receptor potential channel 6 (diacylglycerol-activated non-selective cation channel)/TRPC6	603652	NM_004621	11q21-q22
		solute carrier family 12, member 3/SLC12A3 (renal sodium/chloride transporter)	600968	NM_000339	16q13
	Angiotensin	renin/REN	179820	NM_000537	Xq28
		renin-binding protein/RENBP	312420	NM_002910	1q32
		angiotensinogen/AGT	106150	NM_000029	1q42-q43
		angiotensin II type 1 receptor/AGTR1	106165	M87290	3q21-q25
		guanine nucleotide binding protein (G protein), beta polypeptide 3/GNB3	139130	NM_002075	12p13
		dipeptidyl carboxypeptidase 1 (angiotensin I converting enzyme)/ACE/DCPI	106180	NM_000789	17q23
	Natriuretic Peptide	atrial natriuretic peptide precursor A/NPPA	108780	X01471	1p36.2
		atrial natriuretic peptide precursor B/NPPB	600295	*****	1p36.2
		atrial natriuretic peptide precursor C/NPPC	600296	D28874	2q24-qter
		natriuretic peptide receptor A/ANPRA/NPR1	108960	*****	1q21-q22
		natriuretic peptide receptor B/ANPRB/NPR2	108961	*****	9p21-p12

Blood Pressure Regulation <i>(additional genes in Cardiovascular and Renal)</i>	Endothelin	natriuretic peptide receptor C/ANPRC/NPR3	108962	NM_000908	5p14-p12
		endothelin 1/EDN1	131240	NM_001955	6p24-p23
		endothelin 2/EDN2	131241	NM_001956	1p34
		endothelin 3/EDN3	131242	NM_000114	20q13.2-q13.3
	Vasopressin	endothelin converting enzyme 1/ECE1	600423	NM_001397	1p36.1
		endothelin A receptor isoform delta 3/EDNRA	131243	AF014826	Chr.4
		endothelin receptor type B/EDNRB	131244	NM_000115	13q22
		arginine vasopressin (neurophysin II, antidiuretic hormone, diabetes insipidus, neurohypophyseal)/AVP	192340	NM_000490	20p13
	Nitric Oxide Pathway <i>(additional Genes in Cardiovascular and Renal)</i>	arginine vasopressin receptor 1A/AVPR1A	600821	NM_000706	12q14-q15
		arginine vasopressin receptor 1B/AVPR1B	600264	NM_000707	1q32
		arginine vasopressin receptor 2 (nephrogenic diabetes leucyl/cystinyl)	304800	NM_000054	Xq28
			151300	NM_005575	*****
	Nitric Oxide Pathway <i>(additional Genes in Cardiovascular and Renal)</i>	nitric oxide synthetase 1/NOS1	163731	AH001515	2q24.2-q24.3
		nitric oxide synthetase 2A/NOS2A	163730	X85766	17cen-q11.2
		macrophage nitric oxide synthetase 2B/NOS2B	600719	AH006623	17p13.1-q25
		macrophage nitric oxide synthetase 2C/NOS2C	600720	600720	17p13.1-q25
	Nitric Oxide Pathway <i>(additional Genes in Cardiovascular and Renal)</i>	nitric oxide synthetase 3/NOS3	163729	AH001515	7q36
		chondrocyte nitric oxide synthetase 3/NOS4	163728	X73029	*****
		arginase/ARG1	207800	NM_000045	*****

	arginase/ARG2	107830	NM_001172	4q24.1-q24.3
Ion Channels	ATP sensitive potassium inwardly-rectifying channel, subfamily J, member 5/KCNJ5	600734	NM_000890	11q24
	transient receptor potential channel 3 (diacylglycerol-activated non-selective cation channel)/TRPC3	602345	NM_003305	*****
	transient receptor potential channel 6 (diacylglycerol-activated non-selective cation channel)/TRPC6	603652	NM_004621	11q21-q22
	potassium large conductance calcium-activated channel, subfamily M, alpha member 1/KCNMA1	600150	NM_002247	10q22
	potassium large conductance calcium-activated channel, subfamily M, beta member 1/KCNMB1	603951	NM_004137	5q34
	superoxide dismutase 1/SOD1	147450	NM_000454	21q22.1
	superoxide dismutase 2, mitochondrial	147460	X65965	6q25.3
	glutamate-cysteine ligase (gamma-glutamylcysteine synthetase), catalytic (72.8kD)/GLCLC	230450	NM_001498	6p12
	glutathione synthetase/GSS	601002	NM_000178	20q11.2
	catalase/CAT	115500	NM_001752	11p13
Amelioration of Oxidative Stress	Antioxidants and Free Radical Scavengers			
	glutathione peroxidase 1/GPX1	138320	AF029317	3p21.3
	glutathione peroxidase 2 (gastrointestinal)/GPX2	138319	NM_002083	14q24.1:

	glutathione peroxidase 3 (plasma)/GPX3	138321	NM_00208_4	5q32-q33.1
	glutathione peroxidase 4 (phospholipid hydroperoxidase)/GPX4	138322	NM_00208_5	19p13.3
	glutathione peroxidase 5 (epididymal androgen-related protein)/GPX5	603435	NM_00150_9	*****
	apolipoprotein (a), Lp(a)/LPA	152200	NM_005577	6q27
Transport	RBP5/cellular retinoic acid-binding protein 1/CRABP1	180230	NM_004378	15q24
	cellular retinoic acid-binding protein 2/CRABP2	180231	NM_001878	1q21.3
	retinol-binding protein 1,	180260	NM_002899	3q21-q22
	retinol-binding protein 2,	180280	NM_004164	3q21-qter
	retinol-binding protein 3, interstitial/RBP3	180290	NM_002900	10q11.2
	retinol-binding protein 4, interstitial/RBP4	180250	NM_006744	10q24
	serum vitamin D-binding protein/DBP/group-specific component/GC	139200	L10641	4q12
	transthyretin (prealbumin, amyloidosis type I)/TTR	176300	NM_000371	18q11.2-q12.1
	Retinoic acid receptor, alpha/RARA	180240	NM_00096_4	17q12
	Retinoic acid receptor, beta/RARB	180220	NM_00096_5	3p24
	Retinoic acid receptor, gamma/RARG	180190	NM_00096_6	12q13

Adipocyte Differentiation	Retinoids	Receptors and Coactivators	Retinoid X receptor alpha/RXRA	180245	NM_005693	9q34.3
			Retinoid X receptor beta/RXRB	180246	X66424	6p21.3
			Retinoid X receptor gamma/RXRG	180247	U38480	1q22-q23
			RAR-related orphan receptor A/RORA	600825	NM_002943	15q21-q22
			RAR-related orphan receptor B/RORB	601972	*****	15q21-q22
			RAR-related orphan receptor C/RORC	602943	NM_005060	1q21
			nuclear receptor coactivator 2/GRIP1	601993	NM_006540	*****
			silencing mediator for retinoid and thyroid hormone receptors/SMRT	600848	NM_006312	*****
			retinoic and thyroid hormone receptor associated corepressor			
			1/TRAC1/NCOR1	600849	NM_006311	*****
	Catabolism		UDP glycosyltransferase 1/UGT1	191740	NM_001072	Chr. 12
			UDP glycosyltransferase family 2, member B4/UGT2B4	600067	NM_001073	4q13
			UDP glycosyltransferase family 2, member B7/UGT2B7	600068	NM_001074	1q14
			UDP glycosyltransferase 2 family, polypeptide B11/UGT2B11	603064	NM_001073	*****
			UDP glycosyltransferase family 2, member B15/UGT2B15	600069	NM_001076	4q13
			UDP glycosyltransferase family 2, member B17/UGT2B17	601903	NM_001077	1q14
			Peroxisome proliferative activated receptor, alpha/PPARA	170998	NM_005036	22q12-q13.1

Peroxisome Proliferation	Receptors and Coactivators	Peroxisome proliferative activated receptor, delta/PPARD	6E+05	NM_00623 8	1q21.3
		peroxisome proliferative activated receptor, gamma/PPARG	601487	NM_005037	3p25
		CCAAT/enhancer binding protein (C/EBP), alpha/CEBPA	116897	NM_00436 4	19q13.1
		CCAAT/enhancer binding protein (C/EBP), beta/CEBPB	189965	NM_005194	20q13.1
		CCAAT/enhancer binding protein (C/EBP), gamma/CEBPG	138972	NM_00180 6	Chr. 19
		CCAAT/enhancer binding protein (C/EBP), delta/CEBPD	116898	NM_00519 5	8p11.2- p11.1
		CCAAT/enhancer binding protein (C/EBP), epsilon/CEBPE	600749	NM_00180 5	14q11.2
		acetyl-Coenzyme A carboxylase alpha/ACACA	200350	NM_00066 4	17q21
		acetyl-Coenzyme A carboxylase beta/ACACB	601557	NM_00109 3	12q24.1
		acetyl-Coenzyme A acetyltransferase 1 (acetoacetyl Coenzyme A thiolase)/ACAT1	203750	NM_00001 9	11q22.3- q23.1
	Biosynthesis	acetyl-Coenzyme A acetyltransferase 2 (acetoacetyl Coenzyme A thiolase)/ACAT2	100678	NM_00589 1	6q25.3-q26
		ATP citrate lyase/ACLY	108728	NM_00109 6	17q21.1
		glycerol-3-phosphate acyltransferase, mitochondrial/GPAM1	602395	*****	10q24-q26
		fatty acid synthase/FASN	600212	NM_00410 4	17q25

Transport	apolipoprotein A1 of HDL/APOA1	107680	NM_000039	11q23
	apolipoprotein A2/APOA2	107670	NM_001643	1q21-q23
	apolipoprotein A4/APOA4	107690	NM_000482	11q23
	apolipoprotein B (including Ag(x) antigen)/APOB	107730	NM_000384	2p24
	apolipoprotein B mRNA editing enzyme, catalytic polypeptide	600130	NM_005889	12p13.1
	APOBEC1 binding protein/ABBP1/heterogeneous nuclear ribonucleoprotein A/B/HNRPAB	602688	NM_004499	*****
	apolipoprotein C1/APOC1	107710	NM_001645	19q13.2
	apolipoprotein C2/APOC2	207750	NM_000483	19q13.2
	apolipoprotein C3/APOC3	107720	NM_000040	11q23
	apolipoprotein C4/APOC4	600745	NM_001646	19q13.2
	apolipoprotein D/APOD	107740	NM_001647	3q26.2-qter
	apolipoprotein E/APOE	107741	NM_000041	19q13.2
	apolipoprotein F/APOF	107760	NM_001638	Chr.12
	apolipoprotein H (beta-2-glycoprotein I)/APOH	138700	NM_000042	17q23-qter
	apolipoprotein J/clustrin/APOJ/CLU	185430	NM_001831	8p21-p12
	apolipoprotein L/APOL	603743	AF019225	Chr. 22
	pancreatic triglyceride lipase/PNLIP	246600	AH003527	10q26.1
	enterostatin/colipase, pancreatic/CLPS	120105	NM_001832	6pter-p21.1
	low density lipoprotein receptor (familial hypercholesterolemia)/LDLR	143890	NM_000527	9p13.2-p13.1
	low density lipoprotein receptor-related protein 1/LRP1	107770	NM_002332	2q13.1-q13.2
	low density lipoprotein receptor-related protein 2/LRP2	600073	U33837	2q24-q31

Lipid Metabolism and Storage	Lipid Metabolism and Storage	Uptake				
		low density lipoprotein receptor-related protein 5/LRP5	603506	AF077820	11q13.4	
		low density lipoprotein receptor-related protein 8/LRP8	602600	NM_004631	1p34	
		low density lipoprotein receptor-related protein-associated protein	104225	NM_002337	4p16.3	
		oxidized low density lipoprotein receptor/OLR1	602601	NM_002543	12p13-p12	
		very low density lipoprotein receptor/VLDLR	192977	NM_003383	9p24	
		microsomal triglyceride transfer protein large subunit/MTP	157147	NM_000253	4q22-q24	
		sortilin related receptor/SORL1	602005	NM_003105	1q23.2-q24.2	
		plasma cholesterol ester transfer protein/CETP	118470	NM_000078	16q21	
		phospholipid transfer protein/PLTP	172425	NM_006227	20q12-q13.1	
Storage		glycerol-3-phosphate acyltransferase, mitochondrial/GPAM1	602395	*****	10q24-q26	
Release		lipoprotein lipase/LPL	238600	NM_000237	8p22	
		lipase, hepatic/LIPC	151670	NM_000236	15q21-q23	
		adrenergic, beta-3-, receptor/ADRB3	109691	NM_000025	8p12-p11.2	
		lysosomal acid lipase/LIPB	278000	NM_000235	10q24-q25	
		lipase, hormone-sensitive/LIPE	151750	NM_005357	9q13.1-q13.2	
		perilipin/PLIN	170290	NM_002666	15q26	
		fatty acid binding protein 4, adipocyte/FABP4	600434	NM_001442	8q21	
	Fatty acid CoA Ligase, long chain 1/FACL1	152425	*****	3q13		

Coenzyme A Ligases	Fatty acid CoA Ligase, long chain 2/FACL2	152426	*****	4q34-q35
	Fatty acid CoA Ligase, long chain 3/FACL3	602371	NM_00445 7	2q34-q35
	Fatty acid CoA Ligase, long chain 4/FACL4	300157	NM_00445 8	Xq22.3
	Fatty acid CoA Ligase, very long chain 1/FACVL1	603247	NM_00364 5	15q21.2
β -Oxidation	acyl-Coenzyme A dehydrogenase, long	201460	NM_001608	2q34-q35
	acyl-Coenzyme A dehydrogenase, C-4	201450	NM_000016	1p31
	acyl-Coenzyme A dehydrogenase, C-2	201470	NM_000017	12q22-qter
	carnitine palmitoyltransferase I, liver, nuclear gene encoding mitochondrial protein/CPT1A	600528	NM_001876	11q13
	carnitine palmitoyltransferase II, nuclear gene encoding mitochondrial protein/CPT2	600650	NM_000098	1p32
	carnitine/acylcarnitine	212138	NM_000387	3p21.31
	Enoyl-CoA, hydratase/3-hydroxyacyl CoA dehydrogenase/EHHADH	261515	NM_00196 6	3q27
	hydroxyacyl-CoA dehydrogenase/3- ketoacyl-CoA thiolase/enoyl-CoA hydratase, alpha subunit/HADHA	600890	NM_00018 2	2p23
	hydroxyacyl-CoA dehydrogenase/3- ketoacyl-CoA thiolase/enoyl-CoA hydratase, beta subunit/HADHB	143450	NM_00018 3	2p23
	acyl-Coenzyme A oxidase 1/ACOX1 (peroxisomal)	264470	NM_00403 5	17q25
	acyl-Coenzyme A oxidase 2, branched chain/ACOX2 (peroxisomal)	601641	NM_00350 0	3p14.3

		acyl-Coenzyme A dehydrogenase, C-2 to C-3 short chain precursor/ACADS (mitochondrial)	201470	NM_000017	12q22-qter
		acyl-Coenzyme A dehydrogenase, C-4 to C-12 straight chain/ACADM (mitochondrial)	201450	NM_000016	1p31
		acyl-Coenzyme A dehydrogenase, long chain/ACADL (mitochondrial)	201460	NM_001608	2q34-q35
		hydroxyacyl-Coenzyme A dehydrogenase, type II/HADH2	602057	NM_004493	*****
		enoyl-Coenzyme A hydratase I/ECH1 (peroxisomal)	600696	NM_001398	19q13
Regulation (see also <i>parathyroid hormone</i>)		calcitonin/calcitonin gene-related peptide	114130	NM_001741	1p15.2-p15.1
		calcitonin/calcitonin gene-related peptide	114160	X02404	1p15.2-p15.2
		calcitonin receptor/CALCR	114131	NM_001742	7q21.3
		calcitonin receptor-like/CALCRL	114190	NM_005795	*****
		stanniocalcin/STC1	601185	NM_003155	8p21-p11.2
		sodium-calcium exchanger (isoform NCX1)	182305	AF128524	2p23-p22
Uptake		sodium-calcium exchanger (isoform NCX2)	601901	*****	Chr.14
		solute carrier family 12 (sodium/potassium/chloride transporters), member 1/SLC12A1	600839	NM_000338	15q15-q21.1
Efflux		regucalcin (senescence marker protein-30)/RGN	300212	NM_004683	Xp11.2-q11.2
		bone gamma-carboxyglutamate (gla) protein (osteocalcin)/BGLAP	112260	NM_000711	1q25-q31
Calcium Metabolism		matrix gamma-carboxyglutamate (gla) protein/MGP/MGLAP	154870	NM_000900	12p13.1-p12.3

Calcium Homeostasis	Calcium Deposition	gamma-glutamyl carboxylase/GGCX	137167	NM_000821	2p12
		secreted phosphoprotein 1/SPP1/osteopontin	166490	D14813	4q21-q25
Calcium Homeostasis	Bone Growth Factors	secreted phosphoprotein 2/SPP2/osteopontin	147563	NM_004967	4q21-q25
		sialoprotein, bone sialoprotein			
		vitamin D (1,25- dihydroxyvitamin D3) receptor/VDR	601769	NM_000376	12q12-q14
		core binding factor alpha subunit/CBFA1/runt-related transcription factor 2/osteoblast-transcription factor 2	600211	AH005498	6p21
		osteonectin/ON/secreted protein, acidic, cysteine-rich/SPARC	182120	NM_003118	5q31.3-q32
		osteoprotegerin ligand/OPGL/tumor necrosis factor receptor superfamily, member 11a, activator of NFKB/TNFRSF11A	602642	NM_003839	13q14
		bone morphogenetic protein 1/BMP1	112264	NM_006132	8p21
		bone morphogenetic protein 2 precursor/BMP2	112261	NM_001200	20p12
		bone morphogenetic protein 3 (osteogenic) precursor/BMP3	112263	NM_001201	4p14-q21
		bone morphogenetic protein 4/BMP4	112262	NM_001202	14q22-q23
		bone morphogenetic protein 5/BMP5	112265	*****	Chr. 6
		bone morphogenetic protein 6/BMP6	112266	NM_001718	6p24-p23
		osteogenic protein 1/OP1/bone morphogenetic protein 7 precursor/BMP7	112267	NM_001719	Chr.20
		osteogenic protein 2/OP2/bone morphogenetic protein 8 precursor/BMP8	602284	NM_001720	1p35-p32
Calcium Homeostasis	Bone Growth Factors and Receptors				

Receptors	osteoprotegerin/OPG/tumor necrosis factor receptor superfamily, member 11b/TNFRSF11B	602643	NM_002546	8q24
	bone morphogenetic protein receptor, type IA/BMPRIA	601299	NM_004329	10q22.3
	bone morphogenetic protein receptor, type IB/BMPRI B	603248	NM_001203	4q23-q24
	bone morphogenetic protein receptor, type II precursor (serine/threonine kinase)/BMPRII	600799	NM_001204	2q33-q34
	cytochrome P450, subfamily XXVIIIB (25-hydroxyvitamin D-1-alpha-hydroxylase), polypeptide 1/CYP27B1	264700	NM_000785	12q14
Receptors	vitamin D (1,25-dihydroxyvitamin D3) receptor/VDR	601769	NM_000376	12q12-q14
Signalling	nuclear receptor coactivator 2/GRIP1	601993	NM_006540	*****
	vitamin D3 receptor interacting protein/DRIP80	*****	AF105421	*****
	vitamin D3 receptor interacting protein/DRIP92	*****	AF106934	*****
	vitamin D3 receptor interacting protein/DRIP130	*****	AF105332	*****
Metabolism	cytochrome P450, subfamily XXIV (vitamin D 24-hydroxylase)/CYP24	126065	NM_000782	10q13.2-q13.3
	serum vitamin D-binding protein/DBP/group-specific component/GC	139200	L10641	4q12
	calbindin 3, (vitamin D-dependent calcium-binding protein)/CALB3	302020	NM_004057	Xp

Vitamin D

Phosphate Homeostasis	Phosphate Metabolism	Regulation	X-linked hypophosphatemia protein/HYP/phosphate-regulating endopeptidase homolog, X-linked/PHEX/PEX				Xp22.2-p22.1
			307800	Y10196			
Uptake		alkaline phosphatase, liver/bone/kidney/ALPL	171760	NM_000478			1p36.1-p34
		solute carrier family 17 (sodium phosphate), member 1/SLC17A1	182308	NM_005074			6p23-p21.3
		solute carrier family 17 (sodium phosphate), member 2/SLC17A2	182309	NM_003052			5q35
		solute carrier family 17 (sodium phosphate), member 4/SLC17A4	604216	NM_005495			6p22-p21.3
		solute carrier family 20 (phosphate transporter), member 1/SLC20A1	137570	NM_005415			2q11-q14
		type II sodium-dependent phosphate transporter 3b/NAPI-3B/solute carrier family 34, member 2/SLC34A2	604217	NM_006424			*****
		interleukin 1 beta/IL1B	147720	AF043335			2q14
Interleukins		interleukin 1 receptor, type I/IL1R1	147810	NM_000877			2q12
		interleukin 1 receptor, type 2/IL1R2	147811	NM_004633			2q12-q22
		interleukin 6/IL6	147620	AF048692			7p21
		interleukin 6 receptor/IL6R	147880	NM_000565			1q21
Cytokines		transforming growth factor, beta-1/TGFB1	190180	M60315			9q13.1-q13.3
		transforming growth factor, beta-2/TGFB2	190220	NM_003238			1q41

Transforming Growth Factor	transforming growth factor, beta-3/TGFB3	190230	NM_003239	14q24
	transforming growth factor, beta receptor I (activin A receptor type II-like kinase, 53kD)/TGFBRI	190181	NM_004612	9q33-q34
	transforming growth factor, beta receptor II (70-80kD)/TGFBRII	190182	NM_003242	3p22
	transforming growth factor, beta receptor III (betaglycan, 300kD)/TGFBRIII	600742	NM_003243	1p33-p32
Adhesion Molecules	antigen CD51/integrin, alpha-V/vitronectin receptor/CD51/ITGAV	193210	NM_002210	2q31-q32
	integrin, alpha5/fibronectin receptor, alpha subunit/FNRA/ITGA5	135620	NM_002205	12q11-q13
	lymphocyte antigen CD11C/integrin, alpha-X/CD11C/ITGAX	151510	NM_000887	16p11.2
	lymphocyte antigen CD11A/integrin, alpha-L/CD11A/ITGAL	153370	NM_002209	16p11.2
Inflammation (additional genes in Inflammation)	matrix metalloproteinase 1 (interstitial collagenase)/MMP1	120353	NM_002421	11q22-q23
	matrix metalloproteinase-like 1/MMPL1	*****	NM_004142	*****
	matrix metalloproteinase 2 (neutrophil gelatinase)/CLG4/MMP2	120360	AH002654	16q13
	matrix metalloproteinase 3 (stromelysin 1, progelatinase)/MMP3	185250	NM_002422	11q23
	matrix metalloproteinase 8 (neutrophil collagenase)/MMP8	120355	NM_002424	11q21-q22

Adhesion	matrix metalloproteinase 9 (gelatinase B, 92kD gelatinase, 92kD type IV collagenase)/MMP9	120361	NM_004994	11.2-q13.1
	matrix metalloproteinase 10 (stromelysin 2)/MMP10	185260	NM_002425	11q22.3-q23
	matrix metalloproteinase 11 (stromelysin 3)/MMP11	185261	NM_005940	22q11.2
	matrix metalloproteinase 12 (macrophage elastase)/MMP12	601046	NM_002426	1q22.2-q22.3
	matrix metalloproteinase 13 (collagenase 3)/MMP13	600108	NM_002427	11q22.3
	matrix metalloproteinase 14 (membrane-inserted)/MMP14	600754	NM_004995	14q11-q12
	matrix metalloproteinase 15 (membrane-inserted)/MMP15	602261	NM_002428	16q13-q21
	matrix metalloproteinase 16 (membrane-inserted)/MMP16	602262	NM_005941	8q21
	matrix metalloproteinase 17 (membrane-inserted)/MMP17	602285	NM_004141	12q24.33
	matrix metalloproteinase 19/MMP19	601807	NM_002429	12q14
Proteases	matrix metalloproteinase 23A/MMP23A	603320	NM_004659	1p36.3
	matrix metalloproteinase 23B/MMP23B	603321	NM_006983	1p36.3
	matrix metalloproteinase 24 (membrane-inserted)/MMP24	*****	NM_006690	*****

Table 6. Cardiovascular and Renal Gene List

Class	Pathway	Function	Name	OMIM	GID	Locus
Dopamine Pathway		Biosynthesis	aromatic L-Amino Acid	107930	AH005280	7p11
			Decarboxylase/AADC/dopa decarboxylase			
		Receptors	tyrosine hydroxylase/TH	191290	NM_000360	11p15.5
			dopamine receptor D1/DRD1	126449	NM_000794	5q35.1
			dopamine Receptor D2/DRD2	126450	NM_000795	11q23
			dopamine Receptor D3/DRD3	126451	NM_000796	3q13.3
			dopamine receptor D4/DRD4	126452	NM_000797	11p15.5
			dopamine receptor D5/DRD5	126453	NM_000798	4p16.1-p15.3
		Reuptake	solute carrier family 6 member 3/SLC6A3 (dopamine)	126455	NM_001044	5p15.3
		Catabolism	dopamine beta-hydroxylase (dopamine beta-monooxygenase)/DBH	223360	NM_000787	9q34
			catechol-O-methyltransferase/COMT	116790	NM_000754	22q11.2
			monoamine oxidase A, nuclear gene encoding mitochondrial	309850	NM_000240	Xp11.23
			monoamine oxidase B, nuclear gene encoding mitochondrial	309860	NM_000898	Xp11.23
			phenol-preferring sulfotransferase, family 1A, member 1/SULT1A1	171150	NM_001055	16p12.1-p11.2
			phenol-preferring sulfotransferase, family 1A, member 2/SULT1A2	601292	NM_001054	16p12.1-p11.2
			phenol-preferring sulfotransferase, family 1A, member 3/SULT1A3	600641	L19956	16p11.2
		Biosynthesis	dopamine beta-hydroxylase (dopamine beta-monooxygenase)/DBH	223360	NM_000787	9q34
			phenylethanolamine-N-methyltransferase/PNMT	171190	NM_002686	17q21-q22

		tyrosine hydroxylase/TH	191290	NM_000360	11p15.5
Receptors		adrenergic receptor alpha-1A /ADRA1A	104219	NM_000678	Chr.20
		adrenergic receptor alpha-1B	104220	NM_000679	5q33
		adrenergic receptor alpha-1C /ADRA1C	104221	NM_000680	8p21
		adrenergic receptor alpha-1D /ADRA1D	104222	M76446	20p13
		adrenergic receptor alpha-2A (platelet)/ADRA2A	104210	NM_000681	10q24-q26
		adrenergic receptor alpha-2B (hepatic, renal)/ADRA2B	104260	NM_000682	Chr.2
		adrenergic receptor alpha-2C (renal)/ADRA2C	104250	NM_000683	4q16.1
		adrenergic receptor beta-1/ADRB1	109630	NM_000684	10q24-q26
		adrenergic receptor beta-2/ADRB2	109690	NM_000024	5q32-q34
		adrenergic receptor beta-3/ADRB3	109691	NM_000025	8p12-p11.2
Signalling		beta-adrenergic receptor kinase 1/ADRBK1/BARK	109635	NM_001619	11cen-q13
		beta-adrenergic receptor kinase 2/ADRBK2	109636	X69117	22q11
		guanine nucleotide binding protein (G protein), beta polypeptide 2-like 1/GNB2L1	109760	NM_006098	5q11.2-q13
		arrestin, beta 1/ARRB1	107940	NM_004041	11q13
		vesicular amine transporter 2 / VAT2	193001	L09118	10q25
Reuptake		vesicular amine transporter 1/ VAT1	193002	*****	8p21.3
		Solute carrier family 6 , member 5/SLC6A2/NAT1/NET1	163970	NM_001043	16q12.2

**Epinephrine
and Nor-
epinephrine
Pathway**

Catabolism	monamine oxidase A, nuclear gene encoding mitochondrial	309850	NM_000240	Xp11.23
	monamine oxidase B, nuclear gene encoding mitochondrial	309860	NM_000898	Xp11.23
	catechol-O-methyltransferase/COMT	116790	NM_000754	22q11.2
Biosynthesis	choline acetyltransferase/CHAT	118490	NM_003055	10q11.2
	carnitine acetyltransferase/CRAT	600184	NM_004003	9q34.1
	apolipoprotein E	107741	NM_000041	19q13.2
	cholinergic receptor, muscarinic 1/CHRM1	118510	NM_000738	11q13
	cholinergic receptor, muscarinic 1/CHRM2	118493	NM_000739	7q35-q36
	cholinergic receptor, muscarinic 1/CHRM3	118494	U29589	1q41-q44
	cholinergic receptor, muscarinic 1/CHRM4	118495	NM_000741	11p12-p11.2
	cholinergic receptor, muscarinic 1/CHRM5	118496	AF026263	15q26
	cholinergic receptor, nicotinic, alpha polypeptide 1 (muscle) precursor/CHRNA1	100690	NM_000079	2q24-q32
	cholinergic receptor, nicotinic, alpha polypeptide 2 (neuronal)/CHRNA2	118502	NM_000742	Chr.8
	cholinergic receptor, nicotinic, alpha polypeptide 3 (neuronal) precursor/CHRNA3	118503	NM_000743	15q24
	cholinergic receptor, nicotinic, alpha polypeptide 4 (neuronal) precursor/CHRNA4	118504	NM_000744	20q13.2-q13.3

Acetylcholine Pathway	Receptors	cholinergic receptor, nicotinic, alpha polypeptide 5 (neuronal) precursor/CHRNA5	118505	NM_000745	15q24
		cholinergic receptor, nicotinic, alpha polypeptide 6 (neuronal) precursor/CHRNA6	*****	NM_004198	*****
		cholinergic receptor, nicotinic, alpha polypeptide 7 (neuronal) precursor/CHRNA7	118511	NM_000746	15q14
		cholinergic receptor, nicotinic, beta polypeptide 1 (muscle)/CHRNA1	100710	NM_000747	17p12-p11
		cholinergic receptor, nicotinic, beta polypeptide 2 (neuronal)/CHRNA2	118507	NM_000748	1p21
		cholinergic receptor, nicotinic, beta polypeptide 3/CHRNA3	118508	NM_000749	8p11.2
		cholinergic receptor, nicotinic, beta polypeptide 4/CHRNA4	118509	NM_000750	15q24
		cholinergic receptor, nicotinic, epsilon polypeptide/CHRNAE	100725	NM_000080	Chr.17
		cholinergic receptor, nicotinic, delta polypeptide/CHRNA	100720	NM_000751	2q33-q34
		cholinergic receptor, nicotinic, gamma polypeptide/CHRNA	100730	NM_005199	2q33-q34
		solute carrier family 18 (vesicular acetylcholine), member 3/SLC18A3	600336	NM_003055	10q11.2
		acetylcholinesterase (YT blood group) precursor/ACHE	100740	NM_000665	7q22
		butyrylcholinesterase 1/serum cholinesterase 1/BCHE1	177400	NM_000055	3q26.1-q26.2
	Reuptake				
	Catabolism				

butyrylcholinesterase 2/serum	177500	*****	2q33-q35
cholinesterase 2/BCHE2			
aromatic L-Amino Acid			
Decarboxylase/AADC	107930	AH005280	7p11
tryptophan hydroxylase (tryptophan 5-monooxygenase)/TPH	191060	NM_004179	11p15.3-p14
14-3-3 protein tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, eta polypeptide/YWHAH	113508	NM_003405	22q12
14-3-3 protein tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, epsilon polypeptide/YWHAE	*****	NM_006761	*****
14-3-3 protein tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, zeta polypeptide/YWHAZ	601288	NM_003406	2p25.1
14-3-3 protein tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, beta polypeptide/YWHAB	601289	NM_003404	20q13.1
14-3-3 protein tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, theta polypeptide/YWHAQ	*****	NM_006826	*****
G protein-coupled 5-hydroxytryptamine (serotonin)	109760	NM_000524	5q11.2-q13

Biosynthesis

**Serotonin
Pathway**

Receptors

G protein-coupled 5-hydroxytryptamine (serotonin)	182131	NM_000863	6q13
G protein-coupled 5-hydroxytryptamine (serotonin)	312861	U49516	Xq24
G protein-coupled 5-hydroxytryptamine (serotonin)	182133	NM_000864	1p36.3-p34.3
G protein-coupled 5-hydroxytryptamine (serotonin)	182132	NM_000865	6q14-q15
G protein-coupled 5-hydroxytryptamine (serotonin)	182134	L05597	3p12
G protein-coupled 5-hydroxytryptamine (serotonin)	182135	D87030	13q14-q21
G protein-coupled 5-hydroxytryptamine (serotonin)	601122	NM_000867	2q36.3-q37.1
G protein-coupled 5-hydroxytryptamine (serotonin)	312861	NM_000868	Xq24
gated ion channel 5-hydroxytryptamine (serotonin)	182139	NM_000869	1q23.1-q23.2
gated ion channel 5-hydroxytryptamine (serotonin)	*****	NM_006028	*****
G protein-coupled 5-hydroxytryptamine (serotonin)	602164	Y08756	5q31-q33
G protein-coupled 5-hydroxytryptamine (serotonin)	601305	X81411	7q36.1
G protein-coupled 5-hydroxytryptamine (serotonin)	601109	NM_000871	1p36-p35
G protein-coupled 5-hydroxytryptamine (serotonin)	182137	L21195	10q21-q24

Neuro- and Adenosine	Reuptake	solute carrier family 6 (neurotransmitter transporter, serotonin), member 4/SLC6A4	182138	NM_001045	17q11.1-q12
	Catabolism	monoamine oxidase A, nuclear gene encoding mitochondrial	309850	NM_000240	Xp11.23
		monoamine oxidase B, nuclear gene encoding mitochondrial	309860	M69177	Xp11.23
		serotonin N-Acetyltransferase/SNAT	600950	U40347	17q25
	Biosynthesis	tryptophan 2,3-dioxygenase/TDO2	191070	NM_005651	4q31-q32
		adenylosuccinate lyase/ADSL	103050	NM_000026	22q13.1
		adenylosuccinate synthetase/ADSS	103060	NM_001126	1cen-q12
		adenosine A1 receptor (G-protein coupled)/ADORA1	102775	NM_000674	1q32.1
		adenosine A2a receptor (G-protein coupled)/ADORA2A	102776	NM_000675	22q11.2
		adenosine A2b receptor (G-protein coupled)/ADORA2B	600446	NM_000676	17p12-p11.2
		adenosine A3 receptor (G-protein coupled)/ADORA3	600445	NM_000677	1p21-p13
		adenosine A2 receptor- like/ADORA2L1	102777	*****	10q25.3-q26.1
		purinergic receptor P2X, ligand-gated ion channel, 1/P2RX1	600845	NM_002558	*****
		purinergic receptor P2X, ligand-gated ion channel, 3/P2RX3	600843	NM_002559	11q12
	Receptors	purinergic receptor P2X, ligand-gated ion channel, 4/P2RX4	600846	NM_002560	12q24.32
		purinergic receptor P2X, ligand-gated ion channel, 5/P2RX5	602836	NM_002561	*****

Genetic Control of Heart Rate, Vascular Tone, and Renal Function	Pathway	purinergic receptor P2X, ligand-gated ion channel, 7/P2RX7	602566	NM_002562	12q24
		purinergic receptor P2Y (G-protein coupled) 1/P2RY1	601167	NM_002563	3q25
		purinergic receptor P2Y (G-protein coupled) 2/P2RY2	600041	U07225	1q13.5-q14.1
		purinergic receptor P2Y (G-protein coupled) 4/P2RY4	300038	NM_002565	Xq13
		purinergic receptor P2Y (G-protein coupled) 6/P2RY6	602451	NM_004154	11q13.5
		leukotriene B4 receptor/purinergic receptor P2Y (G-protein coupled) 7/P2RY7	601531	NM_000752	14q11.2-q12
		purinergic receptor P2Y (G-protein coupled) 11/P2RY11	602697	NM_002566	*****
		Solute carrier family 29 (nucleosides), member 1/SLC29A1/ENT1	602193	NM_004955	6p21.2-p21.1
		Solute carrier family 29 (nucleosides), member 2/SLC29A2/ENT2	602110	X86681	11q13
		adenosine deaminase	102700	NM_000022	20q13.11
Histaminergic Pathway	Biosynthesis	Histidine Decarboxylase	142704	M60445	15q21-q22
		histamine H1 receptor/HRH1	600167	NM_000861	3p21-p14
	Receptors	histamine H2 receptor/HRH2	142703	AB023486	*****
		histamine H3 receptor/HRH3	*****	NM_007232	*****
		Histamine N-	*****	NM_006895	chr. 2
	Catabolism	Amine oxidase (copper-containing) 2/AOC2	602268	D88213	17q21

Nitric Oxide Pathway	Biosynthesis	Amine oxidase (copper-containing) 3/AOC3	603735	AF054985	17q21
		nitric oxide synthetase 1/NOS1	163731	AH001515	2q24.2-q24.3
General Metabolism for Peptide Hormones	Biosynthesis and Catabolism	nitric oxide synthetase 2A/NOS2A	163730	X85766	17cen-q11.2
		macrophage nitric oxide synthetase 2B/NOS2B	600719	AH006623	17p13.1-q25
		macrophage nitric oxide synthetase 2C/NOS2C	600720	600720	17p13.1-q25
		nitric oxide synthetase 3/NOS3	163729	AH001515	7q36
		chondrocyte nitric oxide synthetase 3/NOS4	163728	X73029	*****
		arginase/ARG1	207800	NM_000045	*****
		arginase/ARG2	107830	NM_001172	4q24.1-q24.2
		guanylate cyclase 1, soluble, beta 2/GU	603695	AF038499	13q14.3
		guanylate cyclase 1, soluble, beta 3/GU	139397	NM_000857	4q32
		guanylate cyclase 1, soluble, alpha 3/G	139396	NM_000856	4q32
General Metabolism for Peptide Hormones	Biosynthesis and Catabolism	guanylate cyclase 1, soluble, alpha 2/G	601244	NM_000855	11q21-q22
		membrane metalloendopeptidase/MME/neutral endopeptidase	120520	NM_000902	3q21-q27
		calpain, large polypeptide L3/CAPN3	114240	NM_000070	5q15.1-q21.1
		leucyl/cystinyl	151300	NM_005575	*****
		carboxypeptidase N polypeptide 1/CPN1	603103	NM_001308	chr. 10
		carboxypeptidase N polypeptide 2/regulatory subunit/CPN2	603104	J05158	8p23-p22
		meprin alpha subunit/MEP1A	600388	NM_005925	6p21.2-p21.1
		meprin beta subunit/MEP1B	600389	NM_005925	8q12.2-q12.3
		prolyl endopeptidase/PREP	600400	NM_002726	6q22

	neuroendocrine convertase 1/NEC1	162150	D73407	5q14-q21
	peptidylglycine alpha-amidating monooxygenase /PAM/NEC2	170270	NM_000919	5q14-q21
	paired basic amino acid cleaving enzyme/PACE/FUR	136950	X04329	15q25-q26
Biosynthesis	Cholecystokinin/CCK	118440	NM_000729	3pter-p21
Receptors	Cholecystokinin A receptor/CCKAR	118444	NM_000730	4p15.2-p15.1
	Cholecystokinin B receptor/CCKBR	118445	NM_000731	1p15.5-p15.4
Biosynthesis	Neuropeptide Y/NPY	162640	NM_000905	7p15.1
Receptors	Neuropeptide Y receptor Y1/NPY1R	162641	NM_000909	4q31.3-q32
	Neuropeptide Y receptor Y2/NPY2R	162642	NM_000910	4q31
	Neuropeptide Y receptor Y3/chemokine receptor	162643	X71635	2q21
	Neuropeptide Y receptor Y5/NPY5R	602001	NM_006174	4q31-q32
	Neuropeptide Y receptor Y6/NPY6R	601770	NM_006173	5q31
Biosynthesis	kininogen/KNG	228960	*****	3q27
	kallikrein 1/KLK1	147910	AH002853	9q13.2-q13.4
Receptor	bradykinin receptor B1/BDKRBI G protein-coupled	600337	NM_000710	4q32.1-q32.2
	bradykinin receptor B2/BDKRBB2 G protein-coupled	113503	NM_000623	4q32.1-q32.2
	X-prolyl aminopeptidase (aminopeptidase P) 2, membrane-bound/XPNIPEP2	300145	NM_003399	Xq25
Catabolism	carboxypeptidase N, polypeptide 1, 50kD/CPN1	603103	NM_001308	Chr.10
	carboxypeptidase N, polypeptide 2, 83kD/CPN2	603104	*****	8p23-p22

Adrenomedullin	Biosynthesis	adrenomedullin/ADM	103275	NM_001124	11p15.4
Angiotensin	Biosynthesis	angiotensinogen/angiotensin I/AGT	106150	NM_000029	1q42-q43
		renin/REN	179820	NM_000537	1q32
		renin-binding protein/RENBP	312420	NM_002910	Xq28
		membrane metalloendopeptidase/MME/neutral endopeptidase	120520	NM_000902	3q21-q27
		thimet oligopeptidase 1/THOP1	601117	NM_003249	19p13.3
		chymase 1, mast cell/CMA1	118938	NM_001836	14q11.2
		angiotensin converting enzyme/dipeptidyl	106180	NM_000789	17q23
		angiotensin receptor 1/AGTR1	106165	NM_000685	3q21-q25
		angiotensin receptor 1B/AGTR1B	600015	NM_004835	*****
		angiotensin receptor-like 1/AGTRL1	600052	NM_005161	11q12
Vasopressin	Receptors	angiotensin receptor-like 2/AGTRL2	601256	NM_005162	*****
		angiotensin receptor 2/AGTR2	300034	NM_000686	Xq22-q23
		X-prolyl aminopeptidase (aminopeptidase P) 2, membrane-bound/XPNPEP2	300145	NM_003399	Xq25
		prolylcarboxypeptidase/PRCP	176785	NM_005040	11q14
		arginine vasopressin (neurophysin II, antidiuretic hormone, diabetes insipidus, neurohypophyseal)/AVP	192340	NM_000490	20p13
		arginine vasopressin receptor 1A/AVPR1A	600821	NM_000706	12q14-q15
		arginine vasopressin receptor 1B/AVPR1B	600264	NM_000707	1q32

		arginine vasopressin receptor 2 (nephrogenic diabetes)	304800	NM_000054	Xq28
	Catabolism	leucyl/cystinyl	151300	NM_005575	*****
	Biosynthesis	prepro-vasoactive intestinal adenylate-cyclase activating polypeptide 1/ADCYAP1	192320	AH003029	6q26-q27
	Vasoactive Intestinal Peptide	vasoactive intestinal peptide receptor 1/VIPR1	102980	NM_001117	18p11
		vasoactive intestinal peptide receptor 2/VIPR2	192321	NM_004624	3p22
		adenylate cyclase activating polypeptide 1 (pituitary) receptor type 1/ADCYAP1R1	601970	NM_003382	7q36.3
		atrial natriuretic peptide precursor A/NPPA	102981	NM_001118	7p14
		natriuretic peptide precursor B/NPPB	108780	X01471	1p36.2
	Biosynthesis	atrial natriuretic peptide precursor C/NPPC	600295	NM_002521	1p36.2
	Natriuretic Peptide	natriuretic peptide receptor A/guanylate cyclase A (atrionatriuretic peptide receptor C)/NPR1	600296	D28874	2q24-qter
		natriuretic peptide receptor B, isoform a/NPR2	108960	NM_000906	1q21-q22
		natriuretic peptide receptor C/guanylate cyclase C (atrionatriuretic peptide receptor C)/NPR3	108961	NM_000907	9p21-p12
		cytochrome P450, subfamily XIB, polypeptide 2 (steroid 11-b- hydroxylase)/CYP11B2	108962	NM_000908	5p14-p12
			124080	NM_000498	8q21
	Synthesis (additional)				

Mineralocorticosteroids (aldosterone, deoxycorticosterone)	<i>genes in steroid hormone metabolism below)</i>	sodium channel, nonvoltage-gated 1 alpha/SCNN1A	600228	NM_001038	12p13
		sodium channel, nonvoltage-gated 1, beta (Liddle syndrome)/SCNN1B	600760	NM_000336	16p13-p12
		sodium channel, nonvoltage-gated 1, gamma/SCNN1G	600761	NM_001039	16p13-p12
		mineralocorticoid receptor/MCR/nuclear receptor subfamily 3, group C, member	600983	NM_000901	4q31.1
Receptor and Coactivators		nuclear receptor coactivator 2/GRIP1	601993	NM_006540	*****
		oxysterol binding protein/OSBP	167040	NM_002556	11q12-q13
		sterol regulatory element binding transcription factor 1/SREBF1	184756	NM_004176	17p11.2
		sterol regulatory element binding transcription factor 2/SREBF2	600481	NM_004599	22q13
Estrogens		steroid receptor coactivator 1/SRC1	602691	NM_003743	2p23
		steroid receptor RNA activator/SRA	603819	AF092038	Chr. 5
		cytochrome P450, subfamily XIX (androgen aromatase)/CYP19	107910	NM_000103	15q21.1
		estrogen receptor 1/ESR1	133430	NM_000125	6q25.1
Receptors		estrogen receptor 2/ESR2	601663	X99101	14q
		estrogen-related receptor	601998	NM_004451	11q12
		estrogen-related receptor beta/ESRRB	602167	NM_004452	14q24.3
		estrogen-prefering	600043	NM_005420	4q13.1
Catabolism		hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 1/HSD3B1	109715	NM_000862	1p13.1

Progestins	Synthesis	hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 2/HSD3B2	201810	NM_000198	1p13.1
	Receptors	progesterone receptor/PGR	264080	NM_000926	11q22
		heat shock 90-kD protein 1, alpha subunit/HSPCA	140571	*****	1q21.2-q22
		heat shock 90-kD protein 1, beta subunit/HSPCB	140572	J04988	6p12
		FK506-binding protein 5/FKBP5	602623	NM_004117	*****
Androgens	Synthesis	steroid-5-alpha-reductase, alpha polypeptide 1 (3-oxo-5 alpha-steroid delta 4-dehydrogenase alpha 1)/SRD5A1	184753	NM_001047	5p15
		hydroxysteroid (17-beta) dehydrogenase 3/HSD17B3	264300	NM_000197	9q22
		cytochrome P450, subfamily XIA (cholesterol side chain cleavage)/CYP11A	118485	NM_000781	15q23-q24
		steroid 5-alpha-reductase 2/SRD5A2	264600	NM_000348	2p23
	Receptor	androgen receptor (dihydrotestosterone receptor)/AR	313700	NM_000044	Xq11-q12
Mediators of Steroid Response	Catabolism	UDP glycosyltransferase 2 family, polypeptide B17/UGT2B17	601903	NM_001077	4q13
		nuclear receptor coactivator 2/GRIP1	601993	NM_006540	*****
	Transcription	oxysterol binding protein/OSBP	167040	NM_002556	11q12-q13
		sterol regulatory element binding transcription factor 1/SREBF1	184756	NM_004176	17p11.2

(common to the steroid hormones)	n Factors	sterol regulatory element binding transcription factor 2/SREBF2	600481	NM_004599	22q13
		steroid receptor coactivator 1/SRC1	602691	NM_003743	2p23
		steroid receptor RNA activator/SRA	603819	AF092038	Chr. 5
		vascular endothelial growth factor/VEGFA	192240	NM_003376	6p12
Vascular Endothelial Growth Factor	Biosynthesis	vascular endothelial growth factor/VEGFB	601398	NM_003377	11q13
		vascular endothelial growth factor/VEGFC	601528	NM_005429	*****
		kinase insert domain receptor/KDR/FLK1/VEGF receptor/VEGFR	191306	AF063657	4q12
		fms-related tyrosine kinase 1 (vascular endothelial growth factor/vascular permeability factor receptor)/FLT1	165070	NM_002019	13q12
Growth Hormone	Biosynthesis	growth hormone/GHI	139250	NM_000515	17q22-q24
	Receptors	growth hormone receptor/GHR	600946	NM_000163	5p13-p12
Endothelin	Biosynthesis	endothelin 1/EDN1	131240	NM_001955	6p24-p23
		endothelin 2/EDN2	131241	NM_001956	1p34
		endothelin 3/EDN3	131242	NM_000114	20q13.2-q13.3
		endothelin converting enzyme 1/ECE1	600423	NM_001397	1p36.1
	Receptors	endothelin A receptor isoform delta 3/EDNRA	131243	AF014826	Chr.4
		endothelin receptor type B/EDNRB	131244	NM_000115	13q22
		protein kinase C beta/PRKCB	176970	X06318	16p11.2
		transforming growth factor, beta-1/TGFB1	190180	M60315	9q13.1-q13.2

Transforming Growth Factor Beta	Biosynthesis	transforming growth factor, beta-2/TGFB2	190220	NM_003238	1q41
		transforming growth factor, beta-3/TGFB3	190230	NM_003239	14q24
Receptors		transforming growth factor, beta receptor I (activin A receptor type II-like kinase, 53kD)/TGFBRI	190181	NM_004612	9q33-q34
		transforming growth factor, beta receptor II (70-80kD)/TGFBRII	190182	NM_003242	3p22
		transforming growth factor, beta receptor III (betaglycan, 300kD)/TGFBRIII	600742	NM_003243	1p33-p32
		heparin-binding growth factor 1/FGF1	131220	NM_000800	5q31
		basic fibroblast growth factor/FGF2	134920	NM_002006	4q25-q27
		fibroblast growth factor 3/FGF3	164950	NM_005247	11q13
		HST oncogene/fibroblast growth factor 4/FGF4	164980	NM_002008	11q13
		fibroblast growth factor-related protein/FGF5	165190	NM_004464	4q21
		fibroblast growth factor 6/FGF6	134921	X57075	12p13
		keratinocyte growth factor/fibroblast growth factor 7/FGF7	148180	NM_002009	15q15-q21.1
Fibroblast Growth Factor	Biosynthesis	fibroblast growth factor 8 (androgen-induced)/FGF8	600483	NM_006119	10q24
		fibroblast growth factor 9 (glia-activating factor)/FGF9	600921	NM_002010	13q11-q12
		fibroblast growth factor 10/FGF10	602115	NM_004465	5p13-p12
		fibroblast growth factor 11/FGF11	601514	NM_004112	17q21
		fibroblast growth factor 12/FGF12	601513	*****	3q28
		fibroblast growth factor 13/FGF13	300070	NM_004114	Xq26.3

Growth Factors	Receptors	fibroblast growth factor 14/FGF14	601515	NM_004115	13q34
		fibroblast growth factor 16/FGF16	603724	NM_003868	*****
		fibroblast growth factor 17/FGF17	603725	NM_003867	8p21
		fibroblast growth factor 18/FGF18	603726	NM_003862	*****
		fibroblast growth factor 19/FGF19	603891	NM_005117	*****
		fibroblast growth factor receptor 1/FGFR1	136350	*****	8p11.2-p11.1
		fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crouzon syndrome, Pfeiffer syndrome, Jackson-Weiss syndrome)/FGFR2	176943	NM_000141	10q26
		fibroblast growth factor receptor 3 (achondroplasia, thanatophoric dwarfism)/FGFR3	134934	NM_005247	4p16.3
		fibroblast growth factor receptor 4/FGFR4	134935	NM_002011	5q35.1-qter
		somatostatin transcription factor 1/STF1/homeodomain transcription factor/insulin promoter factor 1/IPF1	600733	NM_000209	13q12.1
Growth Factors	Biosynthesis	paired box gene 6/PAX6	106210	NM_000280	11p13
		somatostatin/SST	182450	NM_001048	3q28
		preprocratistatin/CORT	602784	NM_001302	1p36
		Somatostatin receptor 1/G protein-coupled/SSTR1	182451	NM_001049	14q13
		Somatostatin receptor 2/SSTR2	182452	NM_001050	17q24
Growth Factors	Somatostatin				

	Receptors	Somatostatin receptor 3/adenyl cyclase coupled/SSTR3	182453	NM_001051	22q13.1
		Somatostatin receptor 4/SSTR4	182454	NM_001052	20p11.2
		Somatostatin receptor 5/SSTR5	182455	NM_001053	16p13.3
Insulin	Biosynthesis	somatostatin transcription factor 1/STF1/homeodomain transcription factor/insulin promoter factor 1/IPF1	600733	NM_000209	13q12.1
		insulin/INS	176730	NM_000207	11p15.5
		sulfonylurea receptor (hyperinsulinemia)/SUR	600509	NM_000352	11p15.1
		beta-cell inward rectifier subunit/BIR/potassium inwardly-rectifying channel, subfamily J, member 11/KCNJ11	600937	D50582	11p15.1
		carboxypeptidase E/CPE	114855	NM_001873	Chr.4
	Receptor	insulin receptor/INSR	147670	NM_000208	19p13.2
		insulin receptor substrate 1/IRS1	147545	NM_005544	2q36
		insulin receptor substrate 2/IRS2	600797	NM_003749	13q34
		insulin receptor substrate 4/IRS4	603510	NM_003604	*****
		amylin/diabetes-associated peptide/DAP/islet amyloid polypeptide/IAPP	147940	NM_000415	12p12.3-p12.1
	Signaling	insulin-degrading enzyme/IDE	146680	NM_004969	10q23-q25
	Metabolism	insulin-like growth factor 1 (somatomedin C)/IGF1	147440	M27544	12q22-q24.1
	Diagnostic				

Biosynthesis	insulin-like growth factor 2 (somatomedin A)/IGF2	147470	NM_000612	11p15.5
	insulin-like growth factor 1 receptor precursor/IGF1R	147370	NM_000875	15q25-q26
Receptors	insulin-like growth factor 2 receptor/IGF2R	147280	NM_000876	6q26
Insulin-Like Growth Factor	insulin-like growth factor binding protein	146730	NM_000596	7p14-p12
	insulin-like growth factor binding protein	146731	M35410	2q33-q34
	insulin-like growth factor binding protein	146732	NM_000598	7p14-p12
	insulin-like growth factor binding protein	146733	Y12508	17q12-q21
	insulin-like growth factor binding protein	146734	AF055033	2q33-q36
	insulin-like growth factor binding protein	146735	M69054	12q13
	insulin-like growth factor binding protein	602867	NM_001553	4q12
	connective tissue growth factor/CTGF	121009	NM_001901	6q23.1
	insulin-like growth factor binding protein	602369	NM_001554	1p22.3
	insulin-like growth factor binding protein	601489	NM_004970	Chr. 16
Catabolism	protease, serine, 11 (IGF binding)/PRSS11	602194	NM_002775	0q25.3-q26.2
Biosynthesis	angiopoietin 1/ANGPT1	601667	NM_00114 ₆	8q22
	angiopoietin 2/ANGPT2	601922	NM_00114 ₇	8p21
	angiopoietin 3/ANGPT3	603874	NM_00467 ₃	*****
	angiopoietin 4/ANGPT4	603705	AF113708	20p13
	angiopoietin 5/ANGPT5	*****	AF152562	*****
Receptors	protein receptor tyrosine kinase, epithelial-specific 2/TIE2/TEK tyrosine kinase, endothelial/TEK	600221	NM_00045 ₉	9p21

Platelet-Derived Growth Factor	Biosynthesis	platelet-derived growth factor alpha polypeptide/PDGFA	173430	NM_002607	7p22
		platelet-derived growth factor beta polypeptide (simian sarcoma viral (v-sis) oncogene homolog)/PDGFB	190040	NM_002608	12q12.3-q13.1
	Receptors	platelet-derived growth factor receptor, alpha polypeptide/PDGFR	173490	NM_006206	4q12
		platelet-derived growth factor receptor, beta polypeptide/PDGFRB	173410	NM_002609	5q31-q32
Phosphodiesterases		phosphodiesterase 1A, calmodulin-dependent/PDE1A	171890	NM_005019	Chr.4
		phosphodiesterase 1B, calmodulin-dependent/PDE1B	171891	NM_000924	12q13
		phosphodiesterase 1C, calmodulin-dependent/PDE1C	602987	NM_005020	*****
		phosphodiesterase 3A, cGMP-inhibited/PDE3A	123805	NM_000921	11p15
		phosphodiesterase 3B, cGMP-inhibited/PDE3B	602047	NM_000922	11p15
		phosphodiesterase 5A, cGMP-specific/PDE5A	603310	NM_001083	4q26
	AMP-Activated Protein Kinases	protein kinase, AMP-activated, alpha 1	602739	NM_006251	5p12
		protein kinase, AMP-activated, beta 1	602740	NM_006253	12q24.1
		protein kinase, AMP-activated, gamma	602742	NM_002733	12q13.1
		protein kinase, AMP-activated, alpha 2 catalytic subunit/PRKAA2	600497	NM_006252	1p31
		protein kinase, AMP-activated, beta 2 non-catalytic subunit/PRKAB2	602741	NM_005399	*****

	protein kinase, ADP-activated, gamma 2 non-catalytic subunit	602743	*****	7q35-q36
cGMP-Dependent Protein Kinases	protein kinase, cGMP-dependent, regulatory, type I/PRKG1	176894	D45864	10q11.2
	protein kinase, cGMP-dependent, type II/PRKG2	601591	NM_006259	4q13.1-q21.1
	protein kinase, cAMP-dependent, regulatory, type I, alpha (tissue specific extinguisher 1)/PRKAR1A	188830	NM_002734	17q23-q24
cAMP-Activated Protein Kinases	protein kinase, cAMP-dependent, regulatory, type I, beta/PRKAR1B	176911	*****	7pter-p22
	protein kinase, cAMP-dependent, regulatory, type II, alpha/PRKAR2A	176910	NM_004157	3p21.3-p21.2
	protein kinase, cAMP-dependent, regulatory, type II, beta/PRKAR2B	176912	NM_002736	7q22
	protein kinase, cAMP-dependent, catalytic, alpha/PRKACA	601639	NM_002730	19p13.1
	protein kinase, cAMP-dependent, catalytic, beta/PRKACB	176892	NM_002731	1p36.1
	protein kinase, cAMP-dependent, catalytic, gamma/PRKACG	176893	NM_002732	9q13
	guanine nucleotide binding protein (G protein), alpha 11 (Gq class)/GNA11	139313	NM_002067	19p13
	guanine nucleotide binding protein (G protein), alpha 13/GNA13	*****	NM_006572	*****
	guanine nucleotide-binding protein (G protein), alpha 14 /GNA14	*****	NM_004297	*****
	guanine nucleotide binding protein (G protein), alpha 15 (Gq class)/GNA15	139314	NM_002068	19p13

guanine nucleotide binding protein (G protein), alpha activating activity polypeptide L, olfactory type/GNAL	139312	NM_00207_1	18p11.22-p11.21
guanine nucleotide binding protein (G protein), alpha activating activity polypeptide O/GNAO1	139311	Y18213	16q13
guanine nucleotide binding protein (G protein), q polypeptide/GNAQ	600998	NM_00207_2	9q21
guanine nucleotide binding protein (G protein), alpha z polypeptide/GNAZ	139160	NM_00207_3	22q11.2
guanine nucleotide binding protein (G protein), beta polypeptide 1/GNB1	139380	*****	1pter-p31.2
guanine nucleotide binding protein (G protein), beta polypeptide 2/GNB2	139390	NM_00527_3	7q21-q27
guanine nucleotide binding protein (G protein), beta polypeptide 2-like 1/GNB2L1/RACK1	176981	NM_00609_8	*****
guanine nucleotide binding protein (G protein), beta polypeptide 3/GNB3	139130	NM_00207_5	12p13
guanine nucleotide binding protein (G protein), beta 5/GNB5	*****	NM_00657_8	*****
guanine nucleotide binding protein (G protein), gamma 3/GNG3	*****	AF188177	*****
guanine nucleotide binding protein (G protein), gamma 4/GNG4	*****	NM_00448_5	*****
guanine nucleotide binding protein (G protein), gamma 5/GNG5	600874	NM_00527_4	1p22
guanine nucleotide binding protein (G protein), gamma 7/GNG7	*****	NM_00514_5	*****

G-Proteins

Second Messengers

	guanine nucleotide binding protein (G protein), gamma 8/GNG8	*****	AF188179	*****
	guanine nucleotide binding protein (G protein), gamma 10/GNG10	*****	NM_004125	*****
	guanine nucleotide binding protein (G protein), gamma 11/GNG11	*****	NM_004126	*****
	guanine nucleotide binding protein (G protein), gamma 12/GNG12	*****	AF188181	*****
G-Protein Modulators	guanine nucleotide binding protein (G protein), alpha stimulating activity polypeptide 1/GNAS1	139320	NM_000516	20q13.2
	guanine nucleotide binding protein (G protein), alpha inhibiting activity polypeptide 1/GNAI1	139310	NM_002069	7q21
	guanine nucleotide binding protein (G protein), alpha inhibiting activity polypeptide 2/GNAI2	139360	NM_002070	3p21
	guanine nucleotide binding protein (G protein), alpha inhibiting activity polypeptide 3/GNAI3	139370	NM_006496	1p13
	guanine nucleotide binding protein (G protein), alpha inhibiting activity polypeptide H/GNAIH	139180	*****	12p13-p12
	v-src avian sarcoma (Schmidt-Ruppin A-2) viral oncogene homolog/SRC	190090	NM_005417	20q12-q13
Protein Tyrosine Kinases	protein kinase C alpha/PRKCA	176960	NM_002737	17q22-q23.2
	protein kinase C beta/PRKCB	176970	X06318	16p11.2

Calcium- and Diacylglycerol- Activated Protein Kinases	protein kinase C, delta/PRKCD	176977	NM_006254	3p
	protein kinase C, epsilon/PRKCE	176975	NM_005400	2p21
	protein kinase C gamma/PRKCG	176980	*****	19q13.4
	protein kinase C, iota/PRKCI	300094	NM_002740	Xq21.3
	protein kinase C, mu/PRKCM	*****	NM_002742	*****
	protein kinase C, theta/PRKCQ	600448	NM_006257	10p15
(Ca++)- Calmodulin- Dependent Protein Phosphatases	protein kinase C, zeta/PRKCZ	176982	NM_002744	*****
	protein phosphatase 3, catalytic subunit A, alpha isoform/PPP3CA	114105	M29550	4q21-q24
	protein phosphatase 3, catalytic subunit A, beta isoform/PPP3CB	114106	M29551	10q21-q22
	protein phosphatase 3, regulatory subunit B, alpha isoform/PPP3CB	601302	*****	2p16-p15
	mitogen activated protein kinase PRKM1/MAPK1/ERK2	176948	NM_002745	22q11.2
	mitogen activated protein kinase PRKM3/MAPK3/ERK1	601795	X60188	16p11.2
Mitogen Activated	mitogen activated protein kinase PRKM4/MAPK4	176949	NM_002747	18q12-q21
	mitogen activated protein kinase PRKM6/MAPK6	602904	NM_002748	*****
	mitogen activated protein kinase PRKM7/MAPK7	602521	NM_002749	17p11.2
	mitogen activated protein kinase JNK1/PRKM8/MAPK8	601158	L26318	*****

**Growth
Control
(additional
genes in
Oncology)**

Mitogen-activated protein kinases	mitogen activated protein kinase JNK2/PRKM9/MAPK9	602896	U09759	5q35
	mitogen activated protein kinase JNK3/PRKM10/MAPK10	602897	U35003	*****
	mitogen activated protein kinase PRKM11/MAPK11	602898	AF031135	*****
	mitogen activated protein kinase SAPK3/MAPK12	602399	NM_002969	22q13.3
	mitogen activated protein kinase PRKM13/MAPK13	602899	NM_002754	*****
	mitogen activated protein kinase SAPK2A/MAPK14	600289	NM_001315	6p21.3-p21.2
	BCL2	151430	M13994	18q21.3
	BCL-X/BCLX	600039	Z23115	*****
	BCL2 associated protein/BAX	600040	L22473	19q13.3-q13.4
	BCL2-antagonist/killer 1/BAK1	600516	NM_001188	6p21.3-p21.2
	BCL2-associated athanogene 1/BAG1	601497	NM_004323	9p12
	BCL2-associated athanogene 2/BAG2	603882	NM_004282	*****
	BCL2-associated athanogene 3/BAG3	603883	AF095193	*****
	BCL2-associated athanogene 4/BAG4	603884	AF095194	*****
	BCL2-associated athanogene 5/BAG5	603885	AF095195	*****
	BCL-X/BCL-2 binding protein/BAD	603167	AF021792	*****
	BCL2-like 1/BCL2L1	600039	NM_001191	*****
	BCL2-like 2/BCL2L2	601931	NM_004050	14q11.2-q12

BCL2-like 11 (apoptosis facilitator)/BCL2L11	603827	NM_006538	*****
BCL2-related protein A1/BCL2A1	601056	Y09397	15q24.3
BCL2-interacting protein harikari/HRK	603447	NM_003806	*****
BCL-2 interacting killer/BIK	603392	U34584	*****
v-raf-1 murine leukemia viral oncogene homolog 1/RAF1	164760	NM_002880	3p25
tumor protein p53/TP53	191170	X02469	17p13.1
superfamily, member 6/FAS/TNFRSF6	134637	NM_000043	10q24.1
nuclear factor kappa-B DNA binding subunit 1/NFKB1	164011	M58603	4q23-q24
nuclear factor kappa-B DNA binding subunit 2/NFKB2	164012	NM_002502	10q24
apoptosis-related cysteine protease 1/caspase 1/CASP1	147678	L27475	11q22.2-q22.3
apoptosis-related cysteine protease 1/caspase 1/CASP2	600639	*****	7q35
apoptosis-related cysteine protease 1/caspase 1/CASP3	600636	NM_004346	4q35, 4q33-q35.1
apoptosis-related cysteine protease 1/caspase 1/CASP4	602664	NM_004347	11q22.2-q22.3
apoptosis-related cysteine protease 1/caspase 1/CASP5	602665	NM_004347	11q22.2-q22.3
apoptosis-related cysteine protease 1/caspase 1/CASP6	601532	NM_001226	4q25-q25
apoptosis-related cysteine protease 1/caspase 1/CASP7	601761	NM_001227	10q25.1-q25.2

Apoptosis

Apoptosis

	apoptosis-related cysteine protease 1/caspase 1/CASP8	601763	NM_001228	2q33-q34
	apoptosis-related cysteine protease 1/caspase 1/CASP9	602234	*****	*****
	apoptosis-related cysteine protease 1/caspase 1/CASP10	601762	NM_001230	2q33-q34
	apoptosis-related cysteine protease 1/caspase 1/CASP13	603653	NM_003723	*****
	ADP-ribosyltransferase (NAD ⁺ ; poly (ADP-ribose) polymerase)/PARP/ADPRT	173870	NM_001618	1q42
	poly (ADP-ribose) glycohydrolase/PARG	603501	NM_003631	10q11.23
	cyclin-dependent kinase (CDK2)	116953	NM_001798	12q13
	cyclin-dependent kinase (CDK3)	123828	NM_001258	17q22-qter
	cyclin-dependent kinase (CDK4)	123829	NM_000075	12q14
	cyclin-dependent kinase (CDK5)	123831	NM_004935	7q36
	cyclin-dependent kinase (CDK6)	603368	NM_001259	7q21-q22
	cyclin-dependent kinase (CDK7)	601955	NM_003157	2p15-cen
	cyclin-dependent kinase (CDK8)	603184	NM_001260	13q12
	cyclin-dependent kinase (CDK9)	603251	NM_001261	9q34.1
	E2F transcription factor 1/E2F1	189971	M96577	20q11.2
Cell Cycle	Cell Cycle			

BNSDOCID: <WO_____0050639A2_I_>

General Steroid Hormone Metabolism (additional genes in Toxicology)	Anabolism				
	steroid-5-alpha-reductase, alpha polypeptide 1 (3-oxo-5 alpha-steroid delta 4-dehydrogenase alpha 1)/SRD5A1	184753	NM_001047	5p15	
	steroid-5-alpha-reductase, alpha polypeptide 2 (3-oxo-5 alpha-steroid delta 4-dehydrogenase alpha 2)/SRD5A2	264600	NM_000348	2p23	
	steroidogenic acute regulatory protein/STAR	600617	NM_000349	8p11.2	
	cytochrome P450, subfamily XIA (cholesterol side chain cleavage)/CYP11A	118485	NM_000781	15q23-q24	
	cytochrome P450, subfamily XVII (steroid 17-alpha-hydroxylase), adrenal hyperplasia/CYP17	202110	NM_000102	10q24.3	
	hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 1/HSD3B1	109715	NM_000862	1p13.1	
	hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 2/HSD3B2	201810	NM_000198	1p13.1	
	dehydroepiandrosterone (DHEA)-preferring sulfotransferase, family 2A, member 1/SULT2A1	125263	NM_003167	19q13.3	
	estrogen-preferring	600043	NM_005420	4q13.1	
	UDP glycosyltransferase 1/UGT1	191740	NM_001072	Chr. 12	
	UDP glycosyltransferase family 2, member B4/UGT2B4	600067	NM_001073	4q13	
	Catabolism				

Biosynthesis	UDP glycosyltransferase family 2, member B7/UGT2B7	600068	NM_001074	1q14
	UDP glycosyltransferase 2 family, polypeptide B11/UGT2B11	603064	NM_001073	*****
	UDP glycosyltransferase family 2, member B15/UGT2B15	600069	NM_001076	4q13
	UDP glycosyltransferase family 2, member B17/UGT2B17	601903	NM_001077	1q14
Biosynthesis	acetyl-Coenzyme A carboxylase alpha/ACACA	200350	NM_000664	17q21
	acetyl-Coenzyme A carboxylase beta/ACACB	601557	NM_001093	12q24.1
	acetyl-Coenzyme A acetyltransferase 1 (acetoacetyl Coenzyme A thiolase)/ACAT1	203750	NM_000019	11q22.3-q23.1
	acetyl-Coenzyme A acetyltransferase 2 (acetoacetyl Coenzyme A thiolase)/ACAT2	100678	NM_005891	6q25.3-q26
	ATP citrate lyase/ACLY	108728	NM_001096	17q21.1
	glycerol-3-phosphate acyltransferase, mitochondrial/GPAM1	602395	*****	10q24-q26
	fatty acid synthase/FASN	600212	NM_004104	17q25
	apolipoprotein A1 of HDL/APOA1	107680	NM_000039	11q23
	apolipoprotein A2/APOA2	107670	NM_001643	1q21-q23
	apolipoprotein A4/APOA4	107690	NM_000482	11q23
Biosynthesis	apolipoprotein B (including Ag(x) antigen)/APOB	107730	NM_000384	2p24

Transport	apolipoprotein B mRNA editing enzyme, catalytic polypeptide	600130	NM_005889	12p13.1
	APOBEC1 binding protein/ABBP1/heterogeneous nuclear ribonucleoprotein A/B/HNRPAB	602688	NM_004499	*****
	apolipoprotein C1/APOC1	107710	NM_001645	19q13.2
	apolipoprotein C2/APOC2	207750	NM_000483	19q13.2...
	apolipoprotein C3/APOC3	107720	NM_000040	11q23
	apolipoprotein C4/APOC4	600745	NM_001646	19q13.2
	apolipoprotein D/APOD	107740	NM_001647	3q26.2-qter
	apolipoprotein E/APOE	107741	NM_000041	19q13.2
	apolipoprotein F/APOF	107760	NM_001638	Chr.12
	apolipoprotein H (beta-2-glycoprotein I)/APOH	138700	NM_000042	17q23-qter
	apolipoprotein J/clustrin/APOJ/CLU	185430	NM_001831	8p21-p12
	apolipoprotein L/APOL	603743	AF019225	Chr. 22
Lipid Metabolism and Storage	pancreatic triglyceride lipase/PNLIP	246600	AH003527	10q26.1
	enterostatin/colipase, pancreatic/CLPS	120105	NM_001832	6pter-p21.1
	high density lipoprotein receptor/CD36 antigen (collagen type I receptor, thrombospondin receptor)-like 1/CD36L1/SRB1	601040	NM_005505	Chr. 12
	cubilin (intrinsic factor-cobalamin receptor) precursor/CUBN	602997	NM_001081	10p12.1
	cholesterol efflux regulatory protein/CE	600046	NM_005502	9q22-q31
	low density lipoprotein receptor (familial hypercholesterolemia)/LDLR	143890	NM_000527	9p13.2-p13.1
	low density lipoprotein receptor-related protein 1/LRP1	107770	NM_002332	2q13.1-q13.2

Uptake	low density lipoprotein receptor-related protein 2/LRP2	600073	U33837	2q24-q31
	low density lipoprotein receptor-related protein 5/LRP5	603506	AF077820	11q13.4
	low density lipoprotein receptor-related protein 8/LRP8	602600	NM_004631	1p34
	low density lipoprotein receptor-related protein-associated protein	104225	NM_002337	4p16.3
	oxidized low density lipoprotein receptor/OLR1	602601	NM_002543	12p13-p12
	very low density lipoprotein receptor/VLDLR	192977	NM_003383	9p24
	microsomal triglyceride transfer protein large subunit/MTP	157147	NM_000253	4q22-q24
	sortilin related receptor/SORL1	602005	NM_003105	1q23.2-q24.2
	plasma cholesterol ester transfer protein/CETP	118470	NM_000078	16q21
	phospholipid transfer protein/PLTP	172425	NM_006227	20q12-q13.1
	glycerol-3-phosphate acyltransferase, mitochondrial/GPAM1	602395	*****	10q24-q26
	lipoprotein lipase/LPL	238600	NM_000237	8p22
	lipase, hepatic/LIPC	151670	NM_000236	15q21-q23
Storage	adrenergic, beta-3-, receptor/ADRB3	109691	NM_000025	8p12-p11.2
	lysosomal acid lipase/LIPB	278000	NM_000235	10q24-q25
	lipase, hormone-sensitive/LIPE	151750	NM_005357	9q13.1-q13.2
	perilipin/PLIN	170290	NM_002666	15q26
	fatty acid binding protein 4, adipocyte/FABP4	600434	NM_001442	8q21
Release				

Coenzyme A Ligases	Fatty acid CoA Ligase, long chain 1/FACL1	152425	*****	3q13
	Fatty acid CoA Ligase, long chain 2/FACL2	152426	*****	4q34-q35
	Fatty acid CoA Ligase, long chain 3/FACL3	602371	NM_00445 7	2q34-q35
	Fatty acid CoA Ligase, long chain 4/FACL4	300157	NM_00445 8	Xq22.3
	Fatty acid CoA Ligase, very long chain 1/FACVLI	603247	NM_00364 5	15q21.2
Ketogenesis	3-hydroxy-3-methylglutaryl- Coenzyme A synthase 2	600234	NM_00551 8	1p13-p12
	acyl-Coenzyme A dehydrogenase, long	201460	NM_001608	2q34-q35
	acyl-Coenzyme A dehydrogenase, C-4	201450	NM_000016	1p31
	acyl-Coenzyme A dehydrogenase, C-2	201470	NM_000017	12q22-qter
	carnitine palmitoyltransferase I, liver, nuclear gene encoding mitochondrial protein/CPT1A	600528	NM_001876	11q13
	carnitine palmitoyltransferase II, nuclear gene encoding mitochondrial protein/CPT2	600650	NM_000098	1p32
	carnitine/acylcarnitine	212138	NM_000387	3p21.31
	enoyl-CoA, hydratase/3-hydroxyacyl CoA dehydrogenase/EHHADH	261515	NM_00196 6	3q27
	hydroxyacyl-CoA dehydrogenase/3- ketoacyl-CoA thiolase/enoyl-CoA hydratase, alpha subunit/HADHA	600890	NM_000018 2	2p23

β-Oxidation	hydroxyacyl-CoA dehydrogenase/3-ketoacyl-CoA thiolase/enoyl-CoA hydratase, beta subunit/HADHB	143450	NM_000183	2p23
	acyl-Coenzyme A oxidase 1/ACOX1 (peroxisomal)	264470	NM_004035	17q25
	acyl-Coenzyme A oxidase 2, branched chain/ACOX2 (peroxisomal)	601641	NM_003500	3p14.3
	acyl-Coenzyme A dehydrogenase, C-2 to C-3 short chain precursor/ACADS (mitochondrial)	201470	NM_000017	12q22-qter
	acyl-Coenzyme A dehydrogenase, C-4 to C-12 straight chain/ACADM (mitochondrial)	201450	NM_000016	1p31
	acyl-Coenzyme A dehydrogenase, long chain/ACADL (mitochondrial)	201460	NM_001608	2q34-q35
	hydroxyacyl-Coenzyme A dehydrogenase, type II/HADH2	602057	NM_004493	*****
	enoyl-Coenzyme A hydratase 1/ECH1 (peroxisomal)	600696	NM_001398	19q13
	cystathionine-beta-synthase/CBS	236200	NM_000071	21q22.3
	cubilin (intrinsic factor-cobalamin receptor) precursor/CUBN	602997	NM_001081	10p12.1
Homocysteine Metabolism	betaine-homocysteine S-methyltransferase/BHMT	602888	NM_001713	*****
	5-methyltetrahydrofolate-homocysteine methyltransferase/methionine	156570	NM_000254	1q43
	S-adenosylhomocysteine hydrolase/AHCY	180960	M61832	20cen-q13.1

			methylenetetrahydrofolate reductase/MTHFR	236250	AH007464	1p36.3
	Purine Nucleotide Cycle	Purine Nucleotide Cycle	adenosine monophosphate deaminase 1 (isoform M)/AMPD1	102770	NM_000036	1p21-p13
			adenylosuccinate synthase/ADSS	103060	NM_001126	1cen-q12
			adenylosuccinate lyase/ADSL	103050	NM_000026	22q13.1
			sarcoglycan, delta (35kD dystrophin-associated glycoprotein)/SGCD	601411	NM_000337	5q33
			phospholamban/PLN	172405	NM_002667	6q22.1
			desmin/DES	125660	NM_001927	2q35
			cofilin 2 (muscle)/CFL2	601443	*****	Chr. 12
			myosin heavy chain 7, cardiac muscle, beta/MYH7	160760	NM_000257	14q12
			cardiac myosin binding protein C/MYBPC3	600958	NM_000256	11p11.2
			tropomyosin 1 (alpha)/TPM1	191010	NM_000366	15q22.1
			troponin C, slow/TNNC1	191040	NM_003280	3p21.3-p14.3
			troponin I, cardiac/TNNI3	191044	NM_000363	19q13.4
			troponin T2, cardiac/TNNT2	191045	NM_000364	1q32
			elastin (supravalvular aortic stenosis, Williams-Beuren syndrome)/ELN	130160	NM_000501	7q11.2
		Cardiac Muscle Function				
		Structural and Contractile Proteins				

Cardiac Muscle Structure and Metabolism	Sarcoplasmic Reticulum Function	ATPase, Ca++ transporting, cardiac muscle, fast twitch 1/ATP2A1	108730	M23114	16p12
		ATPase, Ca++ transporting, cardiac muscle, slow twitch 2/ATP2A2	108740	NM_001681	12q23-q24.1
		ryanodine receptor 2 (cardiac)/RYR2	180902	NM_001035	1q42.1-q43
		calsequestrin 2, fast twitch cardiac muscle/CASQ2	114251	NM_001232	1p13.3-p11
Cardiac Muscle Structure and Metabolism	Mitochondrial Function	mitochondrial tRNA-Leu (UUR)	590050	S55822	mitochondrial
		tafazzin (cardiomyopathy, dilated 3A (X-linked); endocardial fibroelastosis 2; Barth syndrome/TAZ	300069	NM_000116	Xq28
		focal adhesion kinase/FAK/PTK2 protein	600758	NM_005607	8q24-qter
		sapiens potassium inwardly-rectifying channel	600681	NM_000891	Chr. 17
Cardiac Muscle Structure and Metabolism	Channels	G-protein coupled inwardly rectifying potassium channel/GIRK/potassium inwardly-rectifying channel, subfamily J, member 3/KCNJ3	601534	NM_002239	2q24.1
		ATP sensitive potassium inwardly-rectifying channel, subfamily J, member 5/KCNJ5	600734	NM_000890	11q24
		v-Ha-ras Harvey rat sarcoma viral oncogene homolog/HRAS	190020	NM_005343	11p15.5
		v-Ki-ras2 Kirsten rat sarcoma 2 viral oncogene homolog/KRAS2	190070	NM_004985	12p12.1
Cardiac Muscle Structure and Metabolism		neuroblastoma RAS viral (v-ras) oncogene homolog/NRAS	164790	NM_002524	1p13.2
		ras-related C3 botulinum toxin substrate 1	602048	NM_006908	Xq26.2-27.2
		ras-related C3 botulinum toxin substrate 2	602049	NM_002872	2q12.3-q13.2
		ras-related C3 botulinum toxin substrate 3	602050	NM_002873	2q12.3-q13.2

Response to Mechanical Stress	Signaling	ras-related C3 botulinum toxin substrate	602050	NM_005052	17q24-qter
		LIM domain kinase 1/LIMK1	601329	NM_002314	7q11.23
		LIM domain kinase 2/LIMK2	601988	NM_005569	22q12
		cell division cycle 42 (GTP-binding protein)	116952	NM_001791	1p36.1
		p21/Cdc42/Rac1-activated kinase 1 (yeast Ste20-related)/PAK1	602590	NM_002576	11q13-q14
		protein kinase C-like 2/PRKCL2/RAK2	602549	NM_006256	*****
		oligophenin/OPHN3/p21 (CDKN1A)-activated kinase 3/PAK3	300142	NM_002578	Xq21.3-q24
		cardiac-specific homeo box/CSX	600584	NM_004387	5q34
		GATA-binding protein 4/GATA4	600576	NM_002052	8p23.1-p22
		serum response factor (c-fos serum response element-binding transcription factor)/SRF	600589	NM_003131	*****
Growth Factors	Transcription Factors	granulocyte-macrophage colony stimulating factor 2/CSF2	138960	NM_000758	5q31.1
		macrophage-specific colony-stimulating factor/CSF1	120420	AH005300	1p21-p13
		granulocyte colony stimulating factor 3/CSF3	138970	NM_000759	17q11.2-q12
		erythropoietin/EPO	133170	NM_000799	7q21

Erythroipoies is	flt3 ligand/FMS-related tyrosine kinase 3 ligand/FLT3LG	600007	U03858	19q13.3
	thrombopoietin (MLV oncogene ligand, megakaryocyte growth and development factor)/THPO	600044	NM_000460	3q26.3-q27
	granulocyte-macrophage colony stimulating factor 2 receptor, alpha, low-affinity/CSF2RA	306250	NM_006140	Xp22.32
	granulocyte-macrophage colony stimulating factor 2 receptor, beta/CSF2RB	138981	U18373	22q12.2-q13.1
	granulocyte-macrophage colony stimulating factor 2 receptor, alpha, Y chromosomal/CSF2RY	425000	*****	Yp11
	erythropoietin receptor/EPOR	133171	NM_000121	19p13.3-p13.2
	colony stimulating factor 1 receptor/CSFR1	164770	U63963	5q33.2-q33.3
	myeloproliferative leukemia virus oncogene/MPL/thrombopoietin receptor/TPOR	159530	NM_005373	1p34
	Janus kinase 2 (a protein tyrosine kinase)/JAK2	147796	NM_004972	9p24
	STAM-like protein containing SH3 and ITAM domains 2/STAM2	*****	NM_005843	*****
Signaling, Transcription, and Translation	ribosomal protein S7/RPS7	603474	NM_001011	19q13.2
	signal transducer and activator of transcription 5A/STAT5A	601511	NM_003152	17q11.2

Factors	BCL-X/BCLX	600039	Z23115	*****
	STAT induced STAT inhibitor 3/SSI-3	604176	NM_003955	*****
	FMS-related tyrosine kinase 3/FLT3	136351	NM_004119	13q12
Iron Uptake	ATP-binding cassette 7 iron transporter/ABCB7	300135	NM_004299	Xq13.1-q13.3
	macrophage protein 2/NRAMP2/solute carrier family 11, member 2/SLC11A2	600523	AB015355	12q13
Iron Transport and Storage	transferrin/TF	190000	NM_001063	3q21
	transferrin receptor (p90, CD71)/TFRC	190010	NM_003234	3q29
	transferrin receptor 2/TFR2	*****	NM_003227	*****
	iron-responsive element-binding protein 1/iron regulatory protein 1 (IRE-BP1/IREB1	147581	M58511	Chr.9
	iron-responsive element-binding protein 2/iron regulatory protein 2 (IRE-BP2/IREB2	147582	M58510	Chr.15
	ferritin, light polypeptide/FTL	134790	NM_000146	19q13.3-q13.4
	ferritin, heavy polypeptide 1/TFH1	134770	NM_002032	11q12-q13
	aminolevulinate, delta-, synthase 1, nuclear gene encoding mitochondrial protein/ALAS1	301300	NM_000688	Xp11.21

**Erythrocyte
Production
and
Maintenance**

Heme Metabolism	Heme Synthesis	aminolevulinate, delta-, synthase 2 (sideroblastic/hypochromic anemia), nuclear gene encoding mitochondrial protein/ALAS2	125290	NM_00003 2	3p21.1
		aminolevulinate, delta-, dehydratase/ALAD	125270	NM_00003 1	9q34
		uroporphyrinogen III synthase (congenital erythropoietic porphyria)/UROS	263700	NM_00037 5	10q25.2- q26.3
		uroporphyrinogen decarboxylase/UROD	176100	NM_00037 4	1p34
		porphobilinogen deaminase/PBGD	176000	AH002926	11q23.3
		protoporphyrinogen oxidase, nuclear gene encoding mitochondrial protein/PPOX	600923	NM_00030 9	1q22
		coproporphyrinogen oxidase (coproporphyrin, harderoporphyrin), nuclear gene encoding mitochondrial protein/CPO	121300	NM_00009 7	3q12
		ferrochelatase (protoporphyrin), nuclear gene encoding mitochondrial protein/FECH	177000	NM_00014 0	18q21.3
		hemoglobin, alpha 1/HBA1	141800	NM_00051 7	16pter- p13.3
Hemoglobin Synthesis	Hemoglobin Synthesis	hemoglobin, alpha 2/HBA2	141850	NM_00055 8	16pter- p13.3
		hemoglobin, beta/HBB	141900	NM_00051 8	11p15.5

Heme Catabolism	serum beta-glycoprotein hemoexin/HPX	142290	AH002827	11p15.5-p15.4
	inducible heme oxygenase (decycling) 1/HMOX1	141250	NM_002133	22q12
	constitutive heme oxygenase (decycling) 2/HMOX2	141251	NM_002134	16p13.3
	phenol and bilirubin UDP-glucuronosyltransferase/UDP glycosyltransferase 1/UGT1	191740	NM_001072	Chr.2
	UDP glycosyltransferase 2 family, polypeptide B4/UGT2B4	600067	AF064200	4q13
	UDP glycosyltransferase 2 family, polypeptide B7/UGT2B7	600068	NM_001074	4q13
	biliverdin reductase A/BLVRA	109750	NM_000712	7p14-cen
	biliverdin reductase B/BLVRB	600941	NM_000713	19q13.13-q13.2
	ATPase, Ca++ transporting, cardiac muscle, fast twitch 1/ATP2A1	108730	M23114	16p12
	ATPase, Ca++ transporting, cardiac muscle, slow twitch 2/ATP2A2	108740	NM_001681	12q23-q24.1
Calcium	ATPase, Ca++ transporting, ubiquitous/ATP2A3	601929	NM_005173	17p13.3
	ryanodine receptor 3 (brain and smooth muscle)/RYR3	180903	NM_001036	15q14-q15
	calcium channel, voltage-dependent, L type, alpha 1C subunit/CACNA1C	114205	NM_000719	12p13.3
	potassium voltage-gated channel, shaker-related subfamily, member 4/KCNK4	176266	NM_002233	11q13.4-q14.1

Cardiac and Vascular Channels	Potassium	potassium voltage-gated channel, Isk-related family, member 1/KCNE1	176261	NM_000219	21q22.1-q22.2
		potassium voltage-gated channel, Isk-related family, member 2/KCNE2	603796	NM_005136	21q22.1
		potassium voltage-gated channel, subfamily H, member 2/KCNH2	152427	NM_000238	7q35-q36
		potassium inwardly-rectifying channel, subfamily J, member 5/KCNJ5	600734	NM_000890	11q24
		potassium voltage-gated channel precursor, KQT-like subfamily, member 1/KCNQ1	192500	NM_000218	11p15.5
	Sodium	sodium channel, nonvoltage-gated 1 alpha/SCNN1A	600228	NM_001038	12p13
		sodium channel, nonvoltage-gated 1, beta (Liddle syndrome)/SCNN1B	600760	NM_000336	16p13-p12
		sodium channel, nonvoltage-gated 1, gamma/SCNN1G	600761	NM_001039	16p13-p12
		sodium channel, voltage-gated, type V, alpha polypeptide (long (electrocardiographic) QT syndrome 3)/SCN5A	600163	NM_000335	3p24-p21
		cystic fibrosis transmembrane conductance regulator/CFTR/ATP-binding cassette, subfamily C, member 7/ABCC7	602421	NM_000492	7q31.2
	Chloride	chloride channel, calcium activated, family member 2/CLCA2	604003	NM_006536	*****
		H+-ATPase beta 1 subunit/ATP6B1	267300	AH007312	2cen-q13

Ion and Water Transport

Acidosis	solute carrier family 4, sodium bicarbonate cotransporter, member 4/SLC4A4	603345	NM_003759	4q21
	solute carrier family 4, sodium bicarbonate cotransporter, member 5/SLC4A5	603318	NM_003788	4q21
	carbonic anhydrase II/CA2	259730	NM_000067	8q22
	carbonic anhydrase IV/CA4	114760	NM_000717	17q23
	carbonic anhydrase XII/CA12	603263	AF051882	15q22
	solute carrier family 4, bicarbonate/chloride anion exchanger, member 1/SLC4A1	109270	NM_000342	17q21-q22
	solute carrier family 9, member A1/SLC9A1 (sodium/hydrogen ion)	107310	M81768	1p36.1-p35
	solute carrier family 9, member A2/SLC9A2 (sodium/hydrogen ion)	600530	NM_003048	2q11.2
	solute carrier family 9, member A3/SLC9A3 (sodium/hydrogen ion)	182307	*****	5p15.3
	solute carrier family 9 (sodium/hydrogen exchanger), isoform 3 regulatory factor 1/SLC9A3R1		NM_004252	
	solute carrier family 9 (sodium/hydrogen exchanger), isoform 3 regulatory factor 2/SLC9A3R2		NM_004785	
	Lithosis	Solute carrier family 13, member 2/SLC13A2 (dicarboxylic acids)	604148	NM_003984

Renal Channels	chloride channel 5/CLCN5	300008	NM_000084	Xp11.22
	chloride channel Ka, kidney/CLCNKA	602024	NM_004070	1p36
	chloride channel Kb, kidney/CLCNKB	602023	NM_000085	1p36
	solute carrier family 12 (sodium/potassium/chloride transporters), member 1/SLC12A1	600839	NM_000338	15q15-q21.1
	solute carrier family 12 (sodium/potassium/chloride transporters), member 2/SLC12A2	600840	NM_001046	5q23.3
	solute carrier family 12 (sodium/chloride transporters), member 2/CLCNKA2	600968	NM_000339	16q13
	ATPase, Na+/K+ transporting, alpha 1 polypeptide/ATP1A1	182310	NM_000701	1p13-p11
	ATPase, Na+/K+ transporting, alpha 1 polypeptide-like/ATP1A1L	182360	NM_001676	13q12.1-q12.3
	ATPase, Na+/K+ transporting, alpha 2 polypeptide/ATP1A2	182340	NM_000702	1q21-q23
	ATPase, Na+/K+ transporting, beta 1 polypeptide/ATP1B1	182330	NM_001677	1q22-q25
	ATPase, Na+/K+ transporting, beta 2 polypeptide/ATP1B2	182331	X16645	17p
	ATPase, Na+/K+ transporting, beta 3 polypeptide/ATP1B3	601867	NM_001679	3q22-q23
	arginine vasopressin receptor 2 (nephrogenic diabetes insipidus 2)	304800	NM_000054	Xq28
	aquaporin 1/AQP1	107776	NM_000385	7p14
	Urine Concentration			
	n			

		aquaporin 2/AQP2	107777	NM_000486	12q13
		aquaporin 3/AQP3	600170	NM_004925	9p13
		aquaporin 6/AQP6	601383	NM_001652	12q13
Vesicle Transport	Cytoskeletal Elements	adducin 1 (alpha subunit)/ADD1	102680	NM_001119	4p16.3
		adducin 2 (beta subunit)/ADD2	102681	AF001597	2p14-p13
		adducin 3 (gamma subunit)/ADD3	601568	D67031	10q24.2-q24.3
Gap Junctions	Gap Junctions	gap junction protein, alpha 1, 43kD (connexin 43)/GJA1	121014	NM_000165	6q21-q23.2
		gap-junction protein alpha 3, 46kD (connexin 46)/GJA3	121015	AF075290	13q11-q12
		gap junction protein, alpha 4, 37kD (connexin 37)/GJA4	121012	NM_002060	1p35.1
		gap junction protein, alpha 5, 40kD (connexin 40)/GJA5	121013	NM_005266	1q21.1
		gap junction protein, alpha 7, 45kD (connexin 45)/GJA7	*****	NM_005497	*****
		gap junction protein, alpha 8, 50kD (connexin 45)/GJA8	600897	NM_005267	1q21.1
		gap junction protein, beta 1, 32kD (connexin 32, Charcot-Marie-Tooth neuropathy, X-linked)/GJB1	304040	NM_000166	Xq13.1
		gap junction protein, beta 2, 26 kD (connexin 26)/GJB2	121011	M86849	13q11-q12

	gap junction protein, beta 3, 31 kD (connexin 31)/GJB3	603324	AF052692	1p35.1
	gap junction protein, beta 5, 31.1 kD (connexin 31.1)/GJB5	*****	AF052693	*****
	gap junction protein, beta 6 (connexin 30)/GJB6	*****	NM_00678 3	*****
	factor I/fibrinogen a, alpha/FGA	134820	NM_000508	4q28
	factor I/fibrinogen b, beta/FGB	134830	AH003492	4q28
	factor I/fibrinogen g, gamma/FGG	134850	NM_000509	4q28
	factor II/prothrombin/F2	176930	F2	11p11-q12
	coagulation factor II (thrombin) receptor/F2R	187930	NM_001992	5q13
	coagulation factor II (thrombin) receptor-like 2/F2RL2	601919	NM_004101	5q13
	coagulation factor II (thrombin) receptor-like 3/F2RL3	602779	NM_003950	19p12
	tissue factor/factor	134390	NM_001993	1p22-p21
	tissue factor pathway inhibitor (lipoprotein-associated coagulation inhibitor)/TFPI	152310	NM_006287	2q31-q32.1
	tissue factor pathway inhibitor	600033	NM_006528	7q22
	factor V/proaccelerin/labile factor/F5	227400	NM_000130	1q23
	factor VII/serum prothrombin conversion accelerator/F7	227500	NM_000131	13q34
	factor VIII/antihemophilic factor/F8	306700	NM_000132	Xq28
	factor IX/Christmas factor/plasma thromboplastic component/hemophilia	306900	NM_000133	Xq27.1-q27.2
	factor X/Stuart factor/F10	227600	NM_000504	13q34
	factor XI/plasma thromboplastin antecedent/F11	264900	NM_000128	4q35

brin Formati

Clotting

Thrombus Formation

factor XII/Hageman factor/F12	234000	NM_000505	5q33-qter
factor XIIIa1/fibrin-stabilizing factor/F13A1	134570	NM_000129	6p25-p24
factor XIIIb/fibrin-stabilizing	134580	*****	1q31-q32.1
prekallikrein/Fletcher factor/kallikrein 3, plasma /KLK3	229000	NM_000892	4q35
kininogen/Flaujeac factor/KNG	228960	NM_000893	3q27
protein S (alpha)/PROS1	176880	NM_000313	3p11.1-q11.2
protein C (inactivator of coagulation factors Va and VIIIa)/PROC	176860	NM_000312	2q13-q14
antithrombin III/AT3		NM_000488	1q23-q25
gamma-glutamyl carboxylase/GGCX	137167	NM_000821	2p12
plasminogen/PLG	173350	NM_000301	6q26
monocyte antigen CD87/plasminogen activator receptor, urokinase type/PLAUR/CD87	173391	NM_002659	19q13
plasminogen activator,	191840	NM_002658	10q24
plasminogen activator-tissue/PLAT	173370	A07197	8p12
plasminogen activator inhibitor, type I (arginine-serpin)/PAI1	173360	X12701	7q21.3-q22
plasminogen activator inhibitor, type II (arginine-serpin)/PAI2	173390	NM_002575	18q21.3
integrin, alpha 2b (platelet glycoprotein IIb of IIb/IIIa complex, antigen CD41B)/ITGA2B	273800	NM_000419	17q21.32
integrin beta chain, beta 3 (platelet glycoprotein IIIa of IIb/IIIa complex, antigen CD61)/ITGB3	173470	NM_000212	17q21.32

Thrombolysis

Adhesion	Clot Adherence	glycoprotein Ib (platelet), alpha polypeptide/GPIBA	231200	NM_000173	17pter-p12
		glycoprotein IX (platelet)/GP9	173515	NM_000174	3q21
		calcium and integrin binding protein/CIB	602293	U82226	15q25.3-q26
		thrombospondin 1/THBS1	188060	NM_003246	15q15
		thrombospondin 2/THBS2	188061	NM_003247	6q27
		thrombospondin 3/THBS3	188062	NM_007112	1q21
		thrombospondin 4/THBS4	600715	NM_003248	5q13
		small inducible cytokine subfamily A (Cys-Cys), member 2/monocyte chemotactic protein 1/MCP1/SCYA2	158105	NM_002982	17q11.2-q12
		macrophage-specific colony-stimulating factor/CSF1	120420	AH005300	1p21-p13
		interleukin 1 alpha/IL1A	147760	M15329	2q14
		interleukin 1 beta/IL1B	147720	AF043335	2q14
		apoptosis-related cysteine protease 1/interleukin 1-beta converting enzyme/ICE/caspase 1/CASP1	147678	NM_001223	11q22.2-q22.3
		interleukin 2/IL2	147680	X01586	4q26-q27
		interleukin 3/IL3	147740	NM_000588	5q31.1
		interleukin 4/IL4	147780	NM_000589	5q31.1

interleukin 5/IL5	147850	NM_000879	5q31.1
interleukin 6/IL6	147620	AF048692	7p21
interleukin 7/IL7	146660	NM_000880	8q12-q13
interleukin 8/IL8	146930	M26383	4q12-q13
interleukin 9/IL9	146931	X17543	5q31.1
interleukin 10/IL10	124092	M57627	1q31-q32
interleukin 11 beta/IL11B	147681	NM_000881	19q13.3-q13.4
interleukin 12A (natural killer cell stimulatory factor 1, cytotoxic lymphocyte maturation factor 1, p35)/IL12A	161560	NM_002187	3p12-q13.2
interleukin 12B/IL12B	161561	NM_000440	5q31.1-q33.1
interleukin 13/IL13	147683	NM_002188	5q31
interleukin 15/IL15	600554	U14407	4q31
interleukin 16/IL16	603035	NM_004513	*****
interleukin 17 (cytotoxic T-lymphocyte-associated serine esterase 3)/IL17	603149	NM_002190	2q31
interleukin 18 (interferon-gamma-inducing factor)/IL18	600953	NM_001562	11q22.2-q22.3
interleukin 1 receptor, type I/IL1R1	147810	NM_000877	2q12
interleukin 1 receptor, type 2/IL1R2	147811	NM_004633	2q12-q22

**Cytokines
and
Cytokine
Receptors**

interleukin 1 receptor-like 2/IL1RL2	*****	NM_003854	*****
interleukin 1 receptor accessory protein/IL1RAP	602626	NM_002182	3q28
B-cell antigen CD25/interleukin 2 receptor, alpha chain/IL2RA/CD25	147730	10p15-p14	10p15-p14
interleukin 2 receptor, beta/IL2RB	146710	NM_000878	22q11.2-q13
interleukin 2 receptor, gamma chain/IL2RG	308380	NM_000206	Xq13
interleukin 3 alpha receptor/IL3RA	308385	M74782	Xp22.3
interleukin 4 receptor precursor/IL4R	147781	NM_000418	16p12.1-p11.2
interleukin 5 receptor alpha/IL5RA	147851	M96652	3p26-p24;
interleukin 6 receptor/IL6R	147880	NM_000565	1q21
interleukin 7 receptor/IL7R	146661	NM_002185	5p13
interleukin 9 receptor/IL9R	300007	NM_002186	Xq28
interleukin 10 receptor, alpha/IL10RA	146933	NM_001558	11q23.3
interleukin 10 receptor beta/IL10RB	*****	NM_000628	*****
interleukin receptor 11 alpha/IL11RA	600939	NM_004512	9p13
interleukin 12 receptor, beta 1/IL12RB1	600939	NM_005535	9p13
interleukin 12 receptor, beta 2/IL12RB2	601642	NM_001559	1p31.2

Cell-Mediated Inflammation

	interleukin 13 receptor, alpha 1/IL13RA1	300119	NM_001560	Chr.X
	interleukin receptor 13 alpha2/IL13A2	300130	X95302	Xq24
	interleukin 15 receptor, alpha/IL15RA	601070	NM_002189	10p15-p14
	interleukin 18 receptor 1/IL18R1	*****	NM_003855	*****
Scavenger Receptors	CD36/thrombospondin receptor/platelet collagen	173510	NM_000072	7q11.2
	CD36 antigen (collagen type I receptor, thrombospondin receptor)-like 1/CD36L1/SRB1	601040	NM_005505	Chr. 12
	CD5 antigen-like (scavenger receptor cysteine rich family)/CD5L	602592	NM_005894	1q21-q23
	acetyl LDL receptor/scavenger receptor expressed by endothelial	*****	NM_003693	*****
	macrophage scavenger receptor 1/MSR1	153622	NM_002445	8p22
	macrophage scavenger receptor 1-like/MSRL1	602728	*****	8p21
	macrophage scavenger receptor type III/SRA	153618	NM_002438	10p13
	mannose receptor, C type 1/MRC1	*****	NM_006039	*****
	endocytic receptor (macrophage mannose receptor family) (KIAA0709)	*****	NM_006039	*****
	toll-like receptor 1/TLR1	601194	NM_003263	4p14
	toll-like receptor 2/TLR2	603028	NM_003264	4q32
	toll-like receptor 3/TLR3	603029	NM_003265	4q35
	toll-like receptor 4/TLR4	603030	NM_003266	9q32-q33
	toll-like receptor 5/TLR5	603031	NM_006068	1q41-q42
Inflammatory Response				

(additional genes in Inflammation)	collectin 34	*****	AB002631	*****
	liver collectin 1/CL-L1	*****	NM_006438	*****
	collectin receptor/complement component C1q receptor/C1QR	120577	*****	
	surfactant, pulmonary-associated protein D/SFTPD	178635	NM_003019	10q23.3
	surfactant, pulmonary-associated protein A1/SFTPA1	178630	NM_005411	10q22.2-q23.1
	myeloperoxidase/MPO	254600	J02694	17q23.1
	eosinophil peroxidase/EPX	131399	NM_000502	*****
Inflammatory Superoxide Generation	PHOX22/cytochrome b-245, alpha polypeptide/CYBA	233690	NM_000101	16q24
	cytochrome b-245, beta polypeptide (chronic granulomatous disease)/CYBB	306400	NM_000397	Xp21.1
	PHOX47/soluble oxidase component II/SOC2/neutrophil cytosolic factor 1/NCF1	233700	NM_000265	7q11.23
	PHOX67/neutrophil cytosolic factor 2/NCF2	233710	NM_000433	1q25
	PHOX40/neutrophil cytosolic factor 4/NCF4	601488	NM_000631	22q13.1
	B-cell antigen CD54/intercellular adhesion molecule 1/ICAM1/CD54	147840	NM_000201	19p13.3-p13.2
	receptor for advanced glycation end products/RAGE/AGER	600214	AJ133822	6p21.3
Adhesion	integrin, alpha 7/ITGA7	600536	NM_002206	12q13
	integrin, alpha 8/ITGA8	604063	L36531	*****

integrin, alpha 9/ITGA9	603963	L24158	3p21.3
antigen CD29/integrin, beta-1/CD29/ITGB1	135630	NM_002211	10p11.2
vascular cell adhesion molecule 1/VCAM1	192225	NM_001078	1p32-p31
complement component 1, R subcomponent/C1R	216950	NM_001733	12p13
complement component 1, S subcomponent/C1S	120580	NM_001734	12p13
complement component 1, Q subcomponent, alpha polypeptide/C1QA	120550	*****	1p36.3-p34.1
complement component 1, Q subcomponent, beta polypeptide/C1QB	120570	*****	1p36.3-p34.1
complement component 1, Q subcomponent, gamma polypeptide/C1QG	120575	*****	1p36.3-p34.1
complement component 1, Q subcomponent binding protein/C1QBP	601269	NM_001212	17p13.3
complement component 1 inhibitor (angioedema, hereditary) /C1INH	106100	NM_000062	11q11-q13.1
complement component 2/C2	217000	NM_000063	6p21.3
complement component 3/C3	120700	NM_000064	19p13.3-p13.2
complement component 4B/C4B	120820	NM_000592	6p21.3
complement component 5/C5	120900	NM_001735	9q34.1

complement component 6/C6	217050	NM_000065	5p13
complement component 7/C7	217070	NM_000587	5p13
complement component 8, alpha polypeptide/C8A	120950	NM_000562	1p32
complement component 8, beta polypeptide/C8B	120960	NM_000066	1p32
complement component 8, gamma polypeptide/C8G	120930	NM_000606	9q34.3
complement component 9/C9	120940	NM_001737	5p13
complement factor H/H factor 1/HF1	134370	NM_000186	1q32
I factor (complement)/IF	217030	NM_000204	4q25
decay-accelerating factor for complement/DAF/CD55	125240	S72858	1q32
perforin 1/preforming protein/PRF1	170280	NM_005041	10q22
leukocyte antigen p18-20/protectin/CD59	107271	M95708	11p13
T-cell antigen CD46/membrane cofactor protein/MCP/measels virus receptor/CD46	120920	Y07713	1q32
erythrocyte antigen CD55/decay-accelerating factor for complement/DAF/CD55	125240	S72858	1q32
leukocyte antigen p18-20/protectin/CD59	107271	M95708	11p13

Classical Pathway

Complement

	erythrocyte antigen CD35/complement receptor CR1 (receptor for components C3b/C4b)/CD35/CR1	120620	AH002679	1q32
	complement component 3a receptor 1/C3AR1	*****	NM_004054	*****
	complement component 4-binding protein, alpha/C4BPA	120830	NM_000715	1q32
	complement component 4-binding protein, beta/C4BPB	120831	NM_000716	1q32
	complement component 5 receptor 1 (C5a ligand)/C5AR1	113995	NM_001736	Chr.19
	antigen CD21/CD21	*****	X98257	*****
	B-factor, properdin/BF	138470	NM_001710	6p21.3
	properdin P factor, complement/PFC	312060	NM_002621	Xp11.4-p11.23
	adipsin/complement factor D precursor/DF	134350	NM_001928	*****
	phospholipase A2 group	172411	NM_000300	1p35
Alternative Pathway	phospholipase A2 group IB/PLA2G1B	172410	NM_000928	12q23-q24.1
	phospholipase A2 group X/PLA2G10	603603	NM_003561	16p13.1-p12
	phospholipase A2 group IVA/PLA2G4A	600522	U08374	1q25
	phospholipase A2 group VI/PLA2G6	603604	AF064594	22q13.1
	phospholipase A2 group IVC/PLA2G4C	603602	NM_003706	chr. 19
	phospholipase A2 group V/PLA2G5	601192	NM_000929	1p36-p34
	phospholipase C, beta 2/PLCB2	604114	NM_004573	15q15
	phospholipase C, beta 3/PLCB3	600230	U26425	11q13
Phospholipase				

Release of Membrane Lipids (common to PAF, leukotriene, and prostaglandin pathways)	es	phospholipase C, beta 4/PLCB4	600810	NM_000933	20p12
		phospholipase C, delta 1/PLCD1	602142	NM_006225	3p22-p21.3
		phospholipase C, epsilon/PLCE	600597	NM_006226	2q33
		phospholipase C, gamma 1 (formerly subtype 148)/PLCG1	172420	NM_002660	20q12-q13.1
		phospholipase C, gamma 2			
		(phosphatidylinositol-specific)/PLCG2	600220	NM_002661	16q24.1
		phospholipase D1, phosphatidylcholine- specific/PLD1	602382	NM_002662	3q26
		phospholipase D2/PLD2	602384	NM_002663	17p13.1
		lysosomal acid lipase/LIPB	278000	NM_000235	10q24-q25
		lipocortin 1/annexin 1/ANXA1	151690	V00546	9q11-q22
Annexins		lipocortin 2/annexin 2/ANXA2	151740	D00017	15q21-q22
		lipocortin 3/annexin 3/ANXA3	106490	M20560	4q21
		lipocortin 5/annexin 5/ANXA4	131230	NM_00115 4	4q26-q28
		lipocortin 7/annexin 7/ANXA1	186360	NM_00403 4	10q21.1- q21.2
Arachidonate Metabolism		arachidonate 12-lipoxygenase, 12R type/ALOX12B	603741	NM_00113 9	17pter- p13.1
		arachidonate 15- lipoxygenase/ALOX15	152392	NM_00114 0	17p13.3
		arachidonate 15-lipoxygenase, second type/ALOX15B	603697	NM_00114 1	*****
		prostaglandin endoperoxide synthetase 1/COX1/PTGS1	176805	AH001520	9q32-q33.3
		prostaglandin endoperoxide synthetase 2/COX2/PTGS2	600262	NM_000963	1q25.2-q25.3
		thromboxane A synthase 1/TBXAS1	274180	EG_D34613	7q34

Vasoactive Mediators of Inflammation	Prostaglandins	Biosynthesis	prostaglandin D2 synthase (hematopoietic)	602598	*****	*****
			prostaglandin D2 synthase (21kD, brain)/PTGDS	176803	M61900	*****
			prostaglandin I2 synthase/prostacyclin synthase/PTGIS	601699	EG_D83393	20q13
			prostaglandin E receptor 1, EP1 subtype/PTGER1	176802	NM_000955	19p13.1
Receptors			prostaglandin E receptor 2, EP2 subtype/PTGER2	176804	*****	5p13.1
			prostaglandin E receptor 3, EP3 subtype/PTGER3	176806	NM_000957	1p31.2
			prostaglandin E receptor 4, EP4 subtype/PTGER4	601586	NM_000958	5p13.1
			prostaglandin F receptor/PTGFR	600563	L24470	1p31.1
			prostaglandin F2 receptor negative regulator/PTGFRN	601204	U26664	1p13.1-q21.3
			prostaglandin I2 receptor/PTGIR/prostacyclin receptor	600022	SEG_HUMIF	19q13.3
			thromboxane A2 receptor/TBXA2R	188070	NM_001060	19p13.3
			solute carrier family 21 (prostaglandin transporter), member 2/SLC21A2	601460	NM_005630	3q21
		Catabolism	15-hydroxyprostaglandin dehydrogenase/HPGD	601688	NM_000860	4q34-q35
			aldo-keto reductase family 1, member C2/AKR1C2	600450	NM_001353	10p15-p14
			arachidonate 5-lipoxygenase/ALOX5	152390	NM_000698	Chr.10

Leukotrienes	Synthesis	arachidonate 5-lipoxygenase-activating protein/FLAP/ALOX5AP	603700	NM_001629	13q12
		leukotriene A4 hydrolase/LTA4H (aminopeptidase)	151570	NM_000895	12q22
		leukotriene C4 synthase/LTC4S	246530	NM_000897	5q35
		Gamma-glutamyltranspeptidase 1/GGT1	231950	J04131	22q11.1-q11.2
		Gamma-glutamyltranspeptidase 2/GGT2	137181	AH002728	22q11.1
	Receptors	Gamma-glutamyltransferase-like activity 1/GGTLA1	137168	NM_004121	*****
		cysteinyl leukotriene receptor 1/CYSLT1	300201	NM_006639	Xq13-q21
		leukotriene b4 receptor (chemokine receptor-like 1)/LTB4R	601531	NM_000752	14q11.2-q12
	Catabolism	renal microsomal dipeptidase/DPEP1	179780	NM_004413	16q24.3
	Biosynthesis	CDP-choline:alkylacetyl glycerol cholinephosphotransferase	*****	*****	*****
Platelet Activating Factor (PAF)	Receptors	platelet activating factor receptor/PTAFR	173393	M88177	1p35-p34.3
		platelet activating factor acetylhydrolase 1/PAFAH1	601690	NM_005084	6p21.2-p12
	Catabolism	platelet activating factor acetylhydrolase, isoform 1B, alpha	601545	NM_000430	17p13.3
		platelet activating factor acetylhydrolase, isoform 1B, beta	602508	NM_002572	11q23
		platelet activating factor acetylhydrolase, isoform 1B, gamma	603074	NM_002573	19q13.1
		platelet activating factor acetylhydrolase, isoform 1B, delta			
		platelet activating factor acetylhydrolase, isoform 1B, epsilon			
		platelet activating factor acetylhydrolase, isoform 1B, zeta			

Amelioration of Oxidative Stress	Antioxidants and Free Radical Scavengers	Antioxidants and Free Radical Scavengers	platelet activating factor acetylhydrolase 2/PAFAH2	602344	NM_00043 7	*****
			superoxide dismutase 1/SOD1	147450	NM_000454	21q22.1
			superoxide dismutase 2, mitochondrial	147460	X65965	6q25.3
			glutamate-cysteine ligase (gamma- glutamylcysteine synthetase), catalytic (72.8kD)/GLCLC	230450	NM_00149 8	6p12
			glutathione synthetase/GSS	601002	NM_00017 8	20q11.2
			catalase/CAT	115500	NM_001752	11p13
			glutathione peroxidase 1/GPX1	138320	AF029317	3p21.3
			glutathione peroxidase 2 (gastrointestinal)/GPX2	138319	NM_00208 3	14q24.1:
			glutathione peroxidase 3 (plasma)/GPX3	138321	NM_00208 4	5q32-q33.1
			glutathione peroxidase 4 (phospholipid hydroperoxidase)/GPX4	138322	NM_00208 5	19p13.3
	Prevention of Lipid Oxidation	Prevention of Lipid Oxidation	glutathione peroxidase 5 (epididymal androgen-related protein)/GPX5	603435	NM_00150 9	*****
			ATX1 (antioxidant protein 1, yeast)	602270	NM_00404 5	5q32-q33
			homolog 1/ATOX1	152200	NM_005577	6q27
			apolipoprotein (a), Lp(a)/LPA			
			paraoxonase 1/PON1 (arylesterase)	168820	NM_00044 6	7q21.3
			paraoxonase 2/PON2	602447	NM_00030 5	7q21.3
			paraoxonase 3/PON3	602720	L48516	7q21.4
			apolipoprotein, Lp(a)/LPA	152200	NM_00557 7	6q27

CONFIDENTIAL

01/20/2000

VARIAGENICS

Table 7. Neurological and Psychiatric Disease Indications		Amyotrophic Lateral Sclerosis	Multiple Sclerosis	Dementia	Parkinson's Disease	Huntington's Disease	Epilepsy	Spasticity
Neuro-transmitters	storage							
	release							
	glutamate							
	serotonin							
	dopamine							
	epinephrine and norepinephrine							
	acetylcholine							
	histamine							
	adenosine							
	GABA							
	glycine							
	taurine							
	melatonin							
	nitric oxide							
	peptide hormone processing							
	opioids							
	oxytocin							
	cholecystokinin							
	neuropeptide Y							
	leptin							
	neurotensin							
	tachykinin							
	bradykinin							

4ctq01_.xls

CONFIDENTIAL

4ctq01.xls

VARIAGENICS

[illegible]

Table 7. Neurological and Psychiatric Disease Indications

Table 7. Neurological and Psychiatric Disease Indications						
Pathway	Anxiety	Depression	Schizophrenia	Migraine	Ischemic Cerebrovascular Disease	Neuralgia and Pain
storage						
release						

CONFIDENTIAL

4ctq01.xls

VARIAGENICS

[illegible]

CONFIDENTIAL

01/20/2000

VARIAGENICS

Cellular Growth, Differentiation, and Maintenance	protein maturation and degradation								
	second messenger cascade								
	growth, differentiation, and apoptosis								
	cytoskeleton								
	secretion								
	adhesion								
	amyloid processing								
	lipid transport and metabolism								
	myelination								
	folate metabolism								

Table 8. Toxicological Indication					
Pathway	Efficacy	Safety			
		Brain Dyscrasias	Cutaneous Toxicity	Systemic Toxicity	Hepatic Toxicity
Absorption and Distribution	Gastrointestinal Drug Metabolism				
	Drug Binding				
	Drug Transport				
Phase I Drug Metabolism (oxidation and reduction)	Monooxygenases (mixed function oxidases)				
	General Oxidases				
	Dehydrogenases				
	Fatty Acid b-Oxidation Reduction				

CONFIDENTIAL

Table 8. Toxicological Indication				
	Pathway	Safety		
		Cardiovascular Toxicity	Pulmonary Toxicity	Renal Toxicity
Absorption and Distribution	Gastrointestinal Drug Metabolism			
	Drug Binding			
	Drug Transport			
	Monooxygenases (mixed function oxidases)			
Phase I Drug Metabolism (oxidation	General Oxidases			
	Dehydrogenases			

CONFIDENTIAL

01/20/2000

VARIAGENICS

reduction)	Fatty Acid b-Oxidation					
	Reduction					
Phase II Drug Metabolism (conjugation and catabolism)	Conjugation					
	Catabolism					
Excretion	Uptake and Renal Tubular Uptake and Concentration					
Organ and Tissue Damage	Protection from Radical Damage					
Immune Response	Mast Cell and T-Cell Response					
	B-Cell Response					
	Myeloid Differentiation					

Table 9. Inflammatory Indication						
Pathway	Arthritis	Asthma	Chronic Obstructive Pulmonary Disease	Autoimmune Disease	Inflammatory Bowel Disease	Immunosuppression
Immune Discrimination (Self vs Non-Self)						
Antigen Presentation and Recognition						



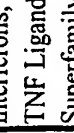
CONFIDENTIAL

Page 716

VARIAGENICS

[illegible]

Table 9. Inflammatory Indication

Pathway	Nephritis	Psoriasis	Atherosclerosis
Antigen Presentation and Recognition			
Interferons, Interleukins, TNF Ligand Superfamily, Chemokine Superfamily, and other Growth Factors			
Cyclophilins			

CONFIDENTIAL

01/20/2000

VARIAGENICS

Cytokine Mediated Immune Regulation	Corticosteroids				
	Testosterone/DHT				
	Vitamin D				
	Retinoic Acid				
	T-Cell, B-Cell, and Myeloid Progenitor Cell Activation, Differentiation, and Proliferation (excluding genes from osteoblast lineage as shown above)				
Cell-Mediated Inflammation	Apoptosis (additional genes in Oncology)				
	Adhesion and Migration				
	Glycosyltransferases				
	Proteases and Protease Inhibitors				
	Phagocytosis or Endocytosis				
Defense Proteins and Peptides	Immunoglobulin Heavy and Light Chains and Genes Involved in Rearrangement, Isotype Switching, and Transcription				
	Complement				
	Acute Protection from Pathogens				

4ctq01_.xls

Page 718

CONFIDENTIAL

01/20/2000

VARIAGENICS

Small Molecule Mediators of Inflammation	Degranulation of Platelets, Mast Cells, Neutrophils, and Eosinophils			
	Release of Membrane Lipids (common to PAF, leukotriene, and prostaglandin pathways)			
	Prostaglandins			
	Platelet Activating Factor (PAF)			
	Lipoxins			
	Leukotrienes			
	Histamine			
	Serotonin			
	Nitric Oxide Pathway			
	Endothelial Growth Factor			
Vascularization	Epinephrine and Norepinephrine Pathway			
	Dopamine Pathway			
Neurotransmitter and Peptide Hormones	Adenosine Pathway			
	Acetylcholine Pathway			
	Ion Channels			
	Opioids			
	Leptin			
	Cholecystokinin (CCK)			

4ctq01_.xls

Page 719

CONFIDENTIAL

01/20/2000

VARIAGENICS

Inflammatory Modulation	Tachykinin, Substance P, or Neurokinin Pathway				
	Bradykinin				
	Parathyroid Hormone (PTH)				
	Melanocortin and Adrenocorticotrophic Hormone				
General Cell Growth	Folate Metabolism				
	Nucleotide Metabolism				
	Cytoskeleton				
	Oxygen Stress (<i>additional genes in Toxicology</i>)				

Table 10. Metabolic or Endocrinologic Indication								
	Pathway	Diabetes Mellitus	Diabetes Insipidus	Obesity	Contra-ception	Hormonal Insufficiency Related to Aging	Osteo-porosis	Acne
General Metabolism for Peptide Hormones	Peptide Hormone Processing							
	Peptide Hormone Control of Metabolism							
Peptide Hormone Control of Metabolism	Circadian Regulation							
	Adrenocorticotrophic Hormone							
	Thyroid Hormone							
	Gonadotropic Hormones							

4ctq01_.xls

Page 720

CONFIDENTIAL

01/20/2000

[illegible]

CONFIDENTIAL

[illegible]

Table 10. Metabolic or Endocrinologic

CONFIDENTIAL

01/20/2000

VARIAGENICS

General Metabolism for Peptide Hormones	Pathway	Alopecia	Adrenal Dysfunction	Thyroid Dysfunction	Parathyroid Dysfunction
Peptide Hormone Control of Metabolism	Peptide Hormone Processing				
	Circadian Regulation				
	Adrenocorticotrophic Hormone				
	Thyroid Hormone				
Steroid Hormones	Gonadotropic Hormones				
	Progestins				
	Estrogens				
	Androgens				
	Glucocorticoids				
	Mineralocorticoids				
	Mediators of Steroid Response				
Neural Regulation of Appetite	Serotonin				
	Dopamine				
	Norepinephrine				
	Neuropeptide Y				
Peptide	Galanin				
	Melanocortin				
	Opioids				
	Cholecystokinin				

CONFIDENTIAL

01/20/2000

VARIAGENICS

Hormonal Regulation of Appetite	Adrenocorticotrophic Hormone				
	PACAP				
	Enterostatin				
	Insulin				
	Leptin				
Control of Metabolism	Thyroid Hormone				
	Glucagon				
	Glucagon-Like Peptide				
Thermo-regulation	Insulin				
	Uncoupling Proteins				
General Growth Control	Somatostatin				
	Growth Hormone				
	Insulin-Like Growth Factor				
	Fibroblast Growth Factor				
	Sonic Hedgehog				
	Nerve Growth Factor				
	Neurotrophins				
	Hormone Signalling				
Carbohydrate Metabolism and Storage	Metabolism				
	Oxytocin				
	Maturation and				
	Protein Glycosylation				
	Neovascularization				
	Hemostasis				
	Amelioration of Oxidative Stress				

4ctq01_.xls

Page 724

VARIAGENICS

01/20/2000

CONFIDENTIAL

Adipocyte Differentiation	Retinoids					
Lipid Metabolism and Storage	Peroxisome Proliferation					
Calcium Homeostasis	Lipid Metabolism and Storage					
Phosphate Homeostasis	Calcium Metabolism					
Inflammation (<i>more genes</i>)	Bone Growth Factors and Receptors					
	Vitamin D					
	Phosphate Metabolism					
	Cytokines					
	Adhesion					

Table 11. Cardiovascular or Renal Indication						
Pathway	Anemia	Atherosclerosis	Angina	Arrhythmia	Hypertension	Ischemia
Dopamine Pathway						
Epinephrine and Norepinephrine Pathway						
Acetylcholine Pathway						
Serotonin Pathway						
Adenosine Pathway						
Histaminergic Pathway						
Nitric Oxide Pathway						
General Metabolism for Peptide Hormones (<i>proteases and glycosylases</i>)						
Cholecystokinin (CCK)						

VARIAGENICS

[illegible]

CONFIDENTIAL

01/20/2000

[illegible]

01/20/2000

VARIAGENICS

[illegible]

Table 11. Cardiovascular or Renal Indication

Table 11. Cardiovascular or Renal Indication					
Pathway	Heart Failure	Thrombosis	Renal Disease	Restenosis	Peripheral Vascular Disease
Dopamine Pathway	+	+	+	+	+
Epinephrine and Norepinephrine Pathway	+	+	+	+	+
Acetylcholine Pathway	+	+	+	+	+
Serotonin Pathway	+	+	+	+	+
Adenosine Pathway	+	+	+	+	+
Histaminergic Pathway	+	+	+	+	+
Nitric Oxide Pathway	+	+	+	+	+
General Metabolism for Peptide Hormones (<i>proteases and glycosylases</i>)	+	+	+	+	+
Cholecystokinin (CCK)	+	+	+	+	+
Neuropeptide Y (NPY)	+	+	+	+	+
Bradykinin	+	+	+	+	+
Adrenomedullin	+	+	+	+	+
Angiotensin	+	+	+	+	+

VARIAGENICS

[illegible]

CONFIDENTIAL

01/20/2000

VARIAGENICS

Cardiac Muscle Structure and Metabolism	Structural and Contractile Proteins						
	Sarcoplasmic Reticulum Function						
	Mitochondrial Function						
	Response to Mechanical Stress						
Erythrocyte Production	Erythropoiesis						
	Heme Metabolism						
Ion and Water Transport	Cardiac and Vascular Channels						
	Renal Channels						
	Vesicle Transport						
	Gap Junctions						
Thrombus Formation	Clotting						
	Clot Adhesion						
Inflammatory Response (additional)	Cell-Mediated Inflammation						
	Complement						
Vasoactive Mediators of Inflammation	Release of Membrane Lipids (common to PAF, leukotrienes, and prostaglandins)						
	Prostaglandins						
	Leukotrienes						
	Platelet Activating Factor (PAF)						

4ctq01_.xls

Page 730





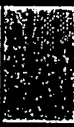



Amelioration of Oxidative Stress	Antioxidants and Free Radical Scavengers					
	Prevention of Lipid Oxidation					

Table 12.
Identified
Variances
In Genes
for
Pathways
Identified
in Cancer
and
Related
Disorders

AB00235	AB00235	603584	GEN- 1CL	Human mRNA for KIAA0358 gene, complete cds	269	82G>A	V28M
AB00235	AB00235	603584	GEN- 1CL	Human mRNA for KIAA0358 gene, complete cds	1567	1380G>A	S
AB00235	AB00235	603584	GEN- 1CL	Human mRNA for KIAA0358 gene, complete cds	1627	1440C>T	S
AB00235	AB00235	603584	GEN- 1CL	Human mRNA for KIAA0358 gene, complete cds	2438	2251G>A	V751M
AB00714	AB00714	603289	GEN-13J	Homo sapiens mRNA for ZIP-kinase, complete cds	360	267G>T	S
AB00714	AB00714	603289	GEN-13J	Homo sapiens mRNA for ZIP-kinase, complete cds	1765	1672G>A	3
AB00787	AB00787	602233	GEN-104	Homo sapiens KIAA0413 mRNA, complete cds	5024	5024G>A	3
AB00787	AB00787	602233	GEN-104	Homo sapiens KIAA0413 mRNA, complete cds	5045	5045G>A	3
AB00787	AB00787	602233	GEN-104	Homo sapiens KIAA0413 mRNA, complete cds	5265	5265T>C	3
AB02068	AB02068	None	GEN- LAX	Homo sapiens mRNA for KIAA0873 protein, partial cds	3854	3854A>G	3
AF001174	AF001174	602898	GEN- 18T	Homo sapiens p38beta2 MAP kinase mRNA, complete cds	1044	1038T>C	S
AF001433	AF001433	601671	GEN-	Human requiem (HREQ)	2378	2337T>C	3

SD-144146.1

AF001900	AF001900	None	18D GEN- 17W	mRNA, complete cds Homo sapiens secreted frizzled-related protein	782	480G>C	S
AF001900	AF001900	None	GEN- 17W	mRNA, complete cds Homo sapiens secreted frizzled-related protein	1668	1366G>A	3
AF004709	AF004709	602899	GEN-UX	mRNA, complete cds Homo sapiens stress- activated protein kinase 4	432	384G>A	S
AF006689	AF006689	603014	GEN-YA	mRNA, complete cds Homo sapiens MAP kinase kinase Jnk2 mRNA,	75	(-1)G>A	5
AF009620	AF009620	601763	GEN- 1HV	complete cds Homo sapiens apoptotic caspase Mch5-beta mRNA, alternatively spliced, complete cds	808	808C>G	H270D
AF009620	AF009620	601763	GEN- 1HV	Homo sapiens apoptotic caspase Mch5-beta mRNA, alternatively spliced, complete cds	915	915G>A	S
AF012535	AF012535	None	GEN- 1Z2	Homo sapiens death receptor 5 (DR5) mRNA, complete cds	234	95T>C	L32P
AF012535	AF012535	None	GEN- 1Z2	Homo sapiens death receptor 5 (DR5) mRNA, complete cds	339	200C>T	A67V
AF012535	AF012535	None	GEN- 1Z2	Homo sapiens death receptor 5 (DR5) mRNA, complete cds	1397	1258G>C	3
AF013988	AF013988	602652	GEN- 20E	Homo sapiens serine protease mRNA, complete cds	271	125C>T	S42L
AF021792	AF021792	603167	GEN- 2A5	Homo sapiens Bcl-X/Bcl-2 binding protein (BAD) mRNA, partial cds	781	781G>A	3
AF021792	AF021792	603167	GEN- 2A5	Homo sapiens Bcl-X/Bcl-2 binding protein (BAD) mRNA, partial cds	883	883C>A	3
AF026070	AF026070	None	GEN- 26S	Homo sapiens death receptor 3 beta (DR3)	455	387A>G	S

SD-144146.1

AF026070	AF026070	None	GEN-26S	mRNA, complete cds	1202	1134T>C	S
				Homo sapiens death receptor 3 beta (DR3)			
AF026070	AF026070	None	GEN-26S	mRNA, complete cds	1204	1136T>G	L379R
				Homo sapiens death receptor 3 beta (DR3)			
AF026070	AF026070	None	GEN-26S	mRNA, complete cds	1237	1169A>G	H390R
				Homo sapiens death receptor 3 beta (DR3)			
AF027706	AF027706	None	GEN-L9F	mRNA, complete cds	1424	1200T>A	S
				Homo sapiens serine/threonine kinase RICK (RICK) mRNA, complete cds			
AF029761	AF029761	None	GEN-MND	Homo sapiens decoy receptor 2 mRNA, complete cds	1011	929C>T	S310L
				untitled			
AF030227	AF030227	164875	GEN-MM5		2702	2605G>A	3
ITGA7	AF032108	600536	GEN-2NO	Homo sapiens integrin alpha-7 mRNA, complete cds	527	366G>A	S
AF035606	AF035606	None	GEN-LCZ	Homo sapiens calcium binding protein (ALG-2) mRNA, complete cds	564	438C>T	S
AF035606	AF035606	None	GEN-LCZ	Homo sapiens calcium binding protein (ALG-2) mRNA, complete cds	1006	880T>C	3
AF036892	AF036892	601937	GEN-7W	Nuclear receptor coactivator (ACTR)	842	659G>T	R220I
AF036892	AF036892	601937	GEN-7W	Nuclear receptor coactivator (ACTR)	1971	1788G>C	Q596H
AF036892	AF036892	601937	GEN-7W	Nuclear receptor coactivator (ACTR)	3048	2865A>G	S
AF036892	AF036892	601937	GEN-7W	Nuclear receptor coactivator (ACTR)	3909	3726A>G	S
AF036892	AF036892	601937	GEN-7W	Nuclear receptor coactivator (ACTR)	4483	4300T>C	3
AF036892	AF036892	601937	GEN-7W	Nuclear receptor coactivator (ACTR)	5644	5461A>G	3
AF036892	AF036892	601937	GEN-7W	Nuclear receptor coactivator (ACTR)	5675	5492T>A	3

SD-144146.1

AF036892	AF036892	601937	GEN-7W	coactivator (ACTR) Nuclear receptor coactivator (ACTR)	6051	5868T>G	3
AF036892	AF036892	601937	GEN-7W	Nuclear receptor coactivator (ACTR)	6664	6481G>A	3
AF053712	AF053712	None	GEN-MM2	Homo sapiens osteoprotegerin ligand mRNA, complete cds	2086	1902T>G	3
AF093771	AF093771	None	GEN-LTJ	Homo sapiens mitoxanthrone resistance protein 1 mRNA, partial sequence	528	529G>A	3
AJ001838	AJ001838	603758	GEN-17S	Homo sapiens mRNA for maleylacetoacetate isomerase	65	(-39)G>C	5
AJ001838	AJ001838	603758	GEN-17S	Homo sapiens mRNA for maleylacetoacetate isomerase	197	94A>G	K32E
AJ001838	AJ001838	603758	GEN-17S	Homo sapiens mRNA for maleylacetoacetate isomerase	227	124G>A	G42R
AJ001838	AJ001838	603758	GEN-17S	Homo sapiens mRNA for maleylacetoacetate isomerase	348	245C>T	T82M
D00017	D00017	151740	GEN-2D	Lipocortin II (Annexin II)	149	100G>A	D34N
D00017	D00017	151740	GEN-2D	Lipocortin II (Annexin II)	341	292G>T	V98L
D00017	D00017	151740	GEN-2D	Lipocortin II (Annexin II)	479	430A>T	N144Y
D00017	D00017	151740	GEN-2D	Lipocortin II (Annexin II)	1288	1239G>A	3
D12614	D12614	153440	GEN-QD	Human mRNA for lymphotoxin (TNF-beta), complete cds	319	179C>A	T60N
D15057	D15057	600243	GEN-1T5	Human mRNA for DAD-1, complete cds	46	(-21)C>T	5
D15057	D15057	600243	GEN-1T5	Human mRNA for DAD-1, complete cds	409	343A>C	3
D15057	D15057	600243	GEN-1T5	Human mRNA for DAD-1, complete cds	464	398G>C	3
D15057	D15057	600243	GEN-1T5	Human mRNA for DAD-1, complete cds	500	434A>G	3
D15057	D15057	600243	GEN-1T5	Human mRNA for DAD-1, complete cds	654	588T>C	3

SD-144146.1

D15057	D15057	600243	GEN-1T5	Human mRNA for DAD-1, complete cds	686	620A>C	3
D25418	D25418	600022	GEN-1T5	Prostaglandin I2 (prostacyclin) receptor (IP)	726	635G>A	R212H
D25418	D25418	600022	GEN-78	Prostaglandin I2 (prostacyclin) receptor (IP)	1047	956C>G	S319W
D25418	D25418	600022	GEN-78	Prostaglandin I2 (prostacyclin) receptor (IP)	1075	984A>C	S
D32051	D32051	138440	GEN-4	Glycinamide ribonucleotide transformylase	25	(-47)G>A	5
D32051	D32051	138440	GEN-4	Glycinamide ribonucleotide transformylase	1332	1261A>G	I421V
D32051	D32051	138440	GEN-4	Glycinamide ribonucleotide transformylase	1855	1784G>C	3
PTGIR	D38128	600022	GEN-4DH	Human IP gene for prostacyclin receptor, exon 3	203	204C>G	3
PTGIR	D38128	600022	GEN-4DH	Human IP gene for prostacyclin receptor, exon 3	231	232C>A	3
D38145	D38145	601699	GEN-4E3	Human mRNA for prostacyclin synthase, complete cds	1646	1619T>C	3
NT5	D38524	129190	GEN-2PF	Human mRNA for 5-nucleotidase	3075	2992C>T	3
D50840	D50840	602874	GEN-314	Human mRNA for ceramide glucosyltransferase, complete cds	638	348T>C	S
D50840	D50840	602874	GEN-314	Human mRNA for ceramide glucosyltransferase, complete cds	1151	861A>G	S
D78586	D78586	114010	GEN-BR	CAD PROTEIN	5308	5282C>A	P1761H
D87461	D87461	601931	GEN-43N	Human mRNA for KIAA0271 gene, complete cds	2432	2256C>A	3
AAC2	D90040	243400	GEN-465	Human mRNA for arylamine N-acetyltransferase (EC	232	191G>A	R64Q

SD-144146.1

AAC2	D90040	243400	GEN-465	Human mRNA for arylamine N- acetyltransferase (EC 2.3.1.5)	323	282C>T	S
AAC2	D90040	243400	GEN-465	Human mRNA for arylamine N- acetyltransferase (EC 2.3.1.5)	844	803A>G	K268R
D90041	D90041	108345	GEN-464	Human liver arylamine N- acetyltransferase (EC 2.3.1.5)	591	445G>A	V149I
D90041	D90041	108345	GEN-464	Human liver arylamine N- acetyltransferase (EC 2.3.1.5) gene	1240	1094C>A	3
DHFR	J00140	126060	GEN- 4E9	Human dihydrofolate reductase gene	721	679T>A	3
DHFR	J00140	126060	GEN- 4E9	Human dihydrofolate reductase gene	721	679T>A	3
DHFR	J00140	126060	GEN- 4E9	Human dihydrofolate reductase gene	829	787C>T	3
J00277	J00277	190020	GEN- MH8	Human (genomic clones lambda-[SK2-T2, HS578T]; cDNA clones RS-[3.4, 6]) c-Ha-ras1 proto-oncogene, complete coding sequence	81	81T>C	S
J03143	J03143	107470	GEN-ZK	Human interferon-gamma receptor mRNA, complete cgs	1098	1050T>G	S
J03209	J03209	185250	GEN-PK	Human matrix metalloproteinase-3 (MMP- 3) mRNA, complete cds	133	133G>A	E45K
J03209	J03209	185250	GEN-PK	Human matrix metalloproteinase-3 (MMP- 3) mRNA, complete cds	288	288C>T	S
J03242	J03242	147470	GEN-PJ	Insulin-like growth factor 2	932	380G>A	R127H
J03242	J03242	147470	GEN-PJ	Insulin-like growth factor 2	1063	511G>A	A171T
J03242	J03242	147470	GEN-PJ	Insulin-like growth factor 2	1190	638C>G	3
J03242	J03242	147470	GEN-PJ	Insulin-like growth factor 2	1201	649C>T	3
J03250	J03250	172420	GEN-C4	DNA topoisomerase I	160	(-52)C>T	5

SD-144146.1

J03250	J03250	172420	GEN-C4	DNA topoisomerase I	590	379G>A	V127I
J03250	J03250	172420	GEN-C4	DNA topoisomerase I	1984	1773G>A	S
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	172	57C>T	S
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	559	444C>T	S
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	1704	1589C>A	3
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	1833	1718C>G	3
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	1959	1844A>C	3
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	3301	3186C>A	3
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	3991	3876A>G	3
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	4187	4072G>A	3
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	4187	4072G>A	3
J03571	J03571	152390	GEN-9	Lipoxigenases: 5-lipoxygenase (leukocytes)	55	21C>T	S
J03571	J03571	152390	GEN-9	Lipoxigenases: 5-lipoxygenase (leukocytes)	304	270G>A	S
J03571	J03571	152390	GEN-9	Lipoxigenases: 5-lipoxygenase (leukocytes)	304	270G>A	S
J03571	J03571	152390	GEN-9	Lipoxigenases: 5-lipoxygenase (leukocytes)	959	925C>A	P309T
J03571	J03571	152390	GEN-9	Lipoxigenases: 5-lipoxygenase (leukocytes)	1762	1728A>T	S
J03571	J03571	152390	GEN-9	Lipoxigenases: 5-lipoxygenase (leukocytes)	2076	2042-2043AC>AC	3

J03571	J03571	152390	GEN-9	Lipoxygenases: 5-lipoxygenase (leukocytes)	2076	2042-2043delAC	F
J03571	J03571	152390	GEN-9	Lipoxygenases: 5-lipoxygenase (leukocytes)	2328	2294C>T	3
J03571	J03571	152390	GEN-9	Lipoxygenases: 5-lipoxygenase (leukocytes)	2376	2342T>G	3
J03626	J03626	258900	GEN-C6	Uridine monophosphate synthetase (orotate phosphoribosyl transferase and orotidine-5-decarboxylase)	742	638G>C	G213A
J03626	J03626	258900	GEN-C6	Uridine monophosphate synthetase (orotate phosphoribosyl transferase and orotidine-5-decarboxylase)	742	638G>C	G213A
J03626	J03626	258900	GEN-C6	Uridine monophosphate synthetase (orotate phosphoribosyl transferase and orotidine-5-decarboxylase)	1424	1320C>T	S
J03626	J03626	258900	GEN-C6	Uridine monophosphate synthetase (orotate phosphoribosyl transferase and orotidine-5-decarboxylase)	1575	1471A>G	3
J03626	J03626	258900	GEN-C6	Uridine monophosphate synthetase (orotate phosphoribosyl transferase and orotidine-5-decarboxylase)	1603	1499delT	F
J03746	J03746	138330	GEN-11Z	Human glutathione S-transferase mRNA, complete cds	560	487A>G	3
J03746	J03746	138330	GEN-11Z	Human glutathione S-transferase mRNA, complete cds	598	525T>G	3
J03817	J03817	138350	GEN-9D	Glutathione S-transferase M1	99	84T>C	S
J03817	J03817	138350	GEN-9D	Glutathione S-transferase M1	543	528C>T	S

SD-144146.1

SD-144146.1

J03817	J03817	138350	GEN-9D	Glutathione S-transferase M1	643	628T>A	S210T
J03817	J03817	138350	GEN-9D	Glutathione S-transferase M1	728	713C>G	3
J03817	J03817	138350	GEN-9D	Glutathione S-transferase M1	902	887C>T	3
J04031	J04031	172460	GEN-CB	Methenyltetrahydrofolate cyclohydrolase	454	401G>A	R134K
J04031	J04031	172460	GEN-CB	Methenyltetrahydrofolate cyclohydrolase	969	916C>G	Q306E
J04031	J04031	172460	GEN-CB	Methenyltetrahydrofolate cyclohydrolase	1614	1561T>C	S
J04031	J04031	172460	GEN-CB	Methenyltetrahydrofolate cyclohydrolase	2011	1958G>A	R653Q
J04031	J04031	172460	GEN-CB	Methenyltetrahydrofolate cyclohydrolase	2335	2282C>T	T761M
J04088	J04088	126430	GEN-8C	Topoisomerase II alpha	543	507G>A	S
J04088	J04088	126430	GEN-8C	Topoisomerase II alpha	1385	1349G>A	R450Q
J04088	J04088	126430	GEN-8C	Topoisomerase II alpha	1474	1438A>G	K480E
J04088	J04088	126430	GEN-8C	Topoisomerase II alpha	1496	1460G>A	R487K
J04088	J04088	126430	GEN-8C	Topoisomerase II alpha	1517	1481G>A	R494Q
J04088	J04088	126430	GEN-8C	Topoisomerase II alpha	1520	1484A>G	E495G
J04088	J04088	126430	GEN-8C	Topoisomerase II alpha	1594	1558A>T	F
J04088	J04088	126430	GEN-8C	Topoisomerase II alpha	2443	2407C>T	P803S
J04088	J04088	126430	GEN-8C	Topoisomerase II alpha	4008	3972A>C	S
J04088	J04088	126430	GEN-8C	Topoisomerase II alpha	4446	4410T>G	S
J04145	J04145	120980	GEN-B	Leukocyte integrin alpha-m	206	206G>A	R69H
J04145	J04145	120980	GEN-B	Leukocyte integrin alpha-m	1780	1780C>T	S
J04145	J04145	120980	GEN-B	Leukocyte integrin alpha-m	2478	2478G>A	S
J04145	J04145	120980	GEN-B	Leukocyte integrin alpha-m	2978	2978C>A	T993N
J04145	J04145	120980	GEN-B	Leukocyte integrin alpha-m	3415	3415C>T	P1139S
J04145	J04145	120980	GEN-B	Leukocyte integrin alpha-m	3661	3661C>T	3
J04145	J04145	120980	GEN-B	Leukocyte integrin alpha-m	3804	3804A>G	3
J04145	J04145	120980	GEN-B	Leukocyte integrin alpha-m	4071	4071G>A	3
GSTM3	J05459	138390	GEN-170	Human glutathione transferase M3 (GSTM3) mRNA, complete cds	687	670G>A	V224I
J05594	J05594	601688	GEN-E	Prostaglandin 15-OH	173	156A>G	S

J05594	J05594	601688	GEN-E	dehydrogenase (PGDH)	913	896C>G	3
J05594	J05594	601688	GEN-E	Prostaglandin 15-OH dehydrogenase (PGDH)	950	933G>A	3
J05594	J05594	601688	GEN-E	Prostaglandin 15-OH dehydrogenase (PGDH)	1448	1431G>A	3
J05594	J05594	601688	GEN-E	Prostaglandin 15-OH dehydrogenase (PGDH)	1972	1955T>C	3
J05594	J05594	601688	GEN-E	Prostaglandin 15-OH dehydrogenase (PGDH)	1972	1955T>C	3
K02286	K02286	191840	GEN-SQ	dehydrogenase (PGDH)	260	260C>G	A87G
K02286	K02286	191840	GEN-SQ	Human urokinase gene, 3 end	449	449G>C	+150S
K02286	K02286	191840	GEN-SQ	Human urokinase gene, 3 end	887	887A>G	Y296C
K02286	K02286	191840	GEN-SQ	Human urokinase gene, 3 end	902	902C>A	P301H
K02286	K02286	191840	GEN-SQ	Human urokinase gene, 3 end	905	905A>G	N302S
K02581	K02581	188300	GEN-CI	Thymidine kinase 1	90	33C>T	S
K02581	K02581	188300	GEN-CI	Thymidine kinase 1	90	33C>T	S
K02581	K02581	188300	GEN-CI	Thymidine kinase 1	112	55G>A	G19R
K02581	K02581	188300	GEN-CI	Thymidine kinase 1	279	222G>A	S
K02581	K02581	188300	GEN-CI	Thymidine kinase 1	282	225G>A	S
K02581	K02581	188300	GEN-CI	Thymidine kinase 1	313	256C>T	F
K02581	K02581	188300	GEN-CI	Thymidine kinase 1	329	272-278TGGCTG	S
K02581	K02581	188300	GEN-CI	Thymidine kinase 1	329	T>TGGCTGT	F
K02581	K02581	188300	GEN-CI	Thymidine kinase 1	334	277G>T	V93F
K02581	K02581	188300	GEN-CI	Thymidine kinase 1	445	388A>G	R130G
K02581	K02581	188300	GEN-CI	Thymidine kinase 1	479	422C>T	P141L
K02581	K02581	188300	GEN-CI	Thymidine kinase 1	487	430G>A	E144K
K02581	K02581	188300	GEN-CI	Thymidine kinase 1	772	715A>G	3
K02581	K02581	188300	GEN-CI	Thymidine kinase 1	867	810G>A	3

K02581	K02581	188300	GEN-CI	Thymidine kinase 1	867	810G>A	3
K02770	K02770	147720	GEN-5M	Interleukin 1, beta	19	(-68)A>C	5
K02770	K02770	147720	GEN-5M	Interleukin 1, beta	26	(-61)A>C	5
K02770	K02770	147720	GEN-5M	Interleukin 1, beta	48	(-39)C>T	5
K02770	K02770	147720	GEN-5M	Interleukin 1, beta	114	28G>A	E10K
K02770	K02770	147720	GEN-5M	Interleukin 1, beta	119	33G>A	M11I
L00634	L00634	134635	GEN-CK	Farnesyltransferase, CAAX box, alpha	182	166G>T	V56L
L00634	L00634	134635	GEN-CK	Farnesyltransferase, CAAX box, alpha	184	168G>A	S
L01087	L01087	600448	GEN-CM	Protein kinase C-theta	1940	1846C>A	S
L01087	L01087	600448	GEN-CM	Protein kinase C-theta	1943	1849G>A	E617K
GSTM5	L02321	138385	GEN- WO	Human glutathione S-transferase (GSTM5) mRNA, complete cds	1406	1349T>C	3
L05628	L05628	158343	GEN-4D9	Human multidrug resistance-associated protein (MRP) mRNA, complete cds	3369	3173G>A	R1058Q
L05628	L05628	158343	GEN-4D9	Human multidrug resistance-associated protein (MRP) mRNA, complete cds	4198	4002G>A	S
TGFBR3	L07594	600742	GEN-1EA	Human transforming growth factor-beta type III receptor (TGF-beta) mRNA, complete cds	3966	3618G>C	3
L07861	L07861	176977	GEN-D0	Protein kinase C, delta	445	387G>A	S
L07861	L07861	176977	GEN-D0	Protein kinase C, delta	1835	1777G>A	V593M
L11284	L11284	176872	GEN-1K8	Homosapiens ERK activator kinase (MEK1) mRNA	1763	1764T>C	3
L11284	L11284	176872	GEN-1K8	Homosapiens ERK activator kinase (MEK1) mRNA	1914	1915G>A	3
L11285	L11285	601263	GEN-1K7	Homosapiens ERK activator kinase (MEK2) mRNA	252	253C>A	3
L11285	L11285	601263	GEN-1K7	Homosapiens ERK activator kinase (MEK2) mRNA	276	277T>C	3

L11285	L11285	601263	GEN-1K7	Homosapiens ERK activator kinase (MEK2) mRNA	537	538C>T	3
L11285	L11285	601263	GEN-1K7	Homosapiens ERK activator kinase (MEK2) mRNA	613	614G>C	3
L11285	L11285	601263	GEN-1K7	Homosapiens ERK activator kinase (MEK2) mRNA	744	745A>C	3
L11285	L11285	601263	GEN-1K7	Homosapiens ERK activator kinase (MEK2) mRNA	1156	1157G>T	3
L11285	L11285	601263	GEN-1K7	Homosapiens ERK activator kinase (MEK2) mRNA	1311	1312C>T	3
L11285	L11285	601263	GEN-1K7	Homosapiens ERK activator kinase (MEK2) mRNA	1457	1458C>A	3
L11285	L11285	601263	GEN-1K7	Homosapiens ERK activator kinase (MEK2) mRNA	1459	1460A>C	3
L12002	L12002	192975	GEN-I	Leukocyte integrin alpha-4 mRNA	1208	798T>C	S
L19182	L19182	602867	GEN-21Z	Human MAC25 mRNA, complete cds	297	284G>A	R95K
L22473	L22473	600040	GEN-L9D	Human Bax alpha mRNA, complete cds	552	552G>A	S
L24470	L24470	600563	GEN-O	PROSTAGLANDIN F RECEPTOR	1422	1185T>C	3
L24470	L24470	600563	GEN-O	PROSTAGLANDIN F RECEPTOR	1490	1253C>T	3
L24470	L24470	600563	GEN-O	PROSTAGLANDIN F RECEPTOR	1517	1280A>G	3
L24470	L24470	600563	GEN-O	PROSTAGLANDIN F RECEPTOR	2244	2007A>G	3
L24470	L24470	600563	GEN-O	PROSTAGLANDIN F RECEPTOR	2299	2062A>G	3
CDA	L27943	123920	GEN-4E4	Homo sapiens cytidine deaminase (CDA) mRNA, complete cds	552	435T>C	S
PTGER2	L28175	601586	GEN-7C	Prostaglandin E receptor 2	547	159C>T	S

PTGER2	L28175	601586	GEN-7C	(subtype EP2), 53kD Prostaglandin E receptor 2	611	223G>A	V75M
PTGER2	L28175	601586	GEN-7C	(subtype EP2), 53kD Prostaglandin E receptor 2	1725	1337A>G	Q446R
L32866	L32866	603352	GEN-2JC	(subtype EP2), 53kD Human effector cell protease receptor-1 (EPR-1) gene, partial cds	308	306A>G	3
L36719	L36719	602315	GEN-2NE	Homo sapiens MAP kinase kinase 3 (MKK3) mRNA, complete cds	1227	890C>A	T297N
L36719	L36719	602315	GEN-2NE	Homo sapiens MAP kinase kinase 3 (MKK3) mRNA, complete cds	1271	934A>G	K312E
GSTT2	L38503	600437	GEN-2PC	Homo sapiens glutathione S-transferase theta 2 (GSTT2) mRNA, complete cds	203	203C>T	S68L
GSTT2	L38503	600437	GEN-2PC	Homo sapiens glutathione S-transferase theta 2 (GSTT2) mRNA, complete cds	543	543C>T	S
L41690	L41690	None	GEN-2T4	Homo sapiens TNF receptor-1 associated protein (TRADD) mRNA, 3 end of cds	399	399G>T	E133D
L41690	L41690	None	GEN-2T4	Homo sapiens TNF receptor-1 associated protein (TRADD) mRNA, 3 end of cds	417	417G>T	E139D
L78207	L78207	600509	GEN-5Q	Cell surface receptor for sulfonylureas on pancreatic b cells	4019	3981A>G	S
M10901	M10901	138040	GEN-2W	Corticosteroid nuclear receptor b	1220	1088A>G	N363S
M10901	M10901	138040	GEN-2W	Corticosteroid nuclear receptor b	2024	1892- 1893AG>AG	S
M10901	M10901	138040	GEN-2W	Corticosteroid nuclear receptor b	2024	1892- 1893delAG	F
M10901	M10901	138040	GEN-2W	Corticosteroid nuclear receptor b	2054	1922A>T	D641V

SD-144146.1

M10901	M10901	138040	GEN-2W	Corticosteroid nuclear receptor b	2372	2240T>G	I747S
M10901	M10901	138040	GEN-2W	Corticosteroid nuclear receptor b	2391	2259A>C	L753F
M10901	M10901	138040	GEN-2W	Corticosteroid nuclear receptor b	2391	2259A>T	L753F
M11050	M11050	138040	GEN-7Y	Glucocorticoid receptor	2166	2034C>T	S
M11050	M11050	138040	GEN-7Y	Glucocorticoid receptor	3353	3221T>G	3
M11050	M11050	138040	GEN-7Y	Glucocorticoid receptor	3398	3266T>G	3
ETS2	M11922	164740	GEN-1LG	Human Hu-ets-2 gene, homologous to avian erythroblastosis virus transforming gene, partial cds	54	54A>G	S
M12674	M12674	133430	GEN-7Z	Estrogen receptor	1267	975C>G	S
M12783	M12783	190040	GEN-QF	Human c-sis/platelet-derived growth factor 2 (SIS/PDGF2) mRNA, complete cds	1896	804T>C	3
M12783	M12783	190040	GEN-QF	Human c-sis/platelet-derived growth factor 2 (SIS/PDGF2) mRNA, complete cds	2148	1056T>C	3
M12783	M12783	190040	GEN-QF	Human c-sis/platelet-derived growth factor 2 (SIS/PDGF2) mRNA, complete cds	2250	1158G>A	3
M13194	M13194	126380	GEN-EA	DNA EXCISION REPAIR PROTEIN ERCC-1	496	354C>T	S
M13194	M13194	126380	GEN-EA	DNA EXCISION REPAIR PROTEIN ERCC-1	1078	936C>T	3
M13509	M13509	120353	GEN-QJ	Human skin collagenase mRNA, complete cds	383	315A>G	S
M13509	M13509	120353	GEN-QJ	Human skin collagenase mRNA, complete cds	899	831G>A	S
M13509	M13509	120353	GEN-QJ	Human skin collagenase mRNA, complete cds	1522	1454A>G	3
M13509	M13509	120353	GEN-QJ	Human skin collagenase mRNA, complete cds	1747	1679C>T	3
BCL2	M13994	151430	GEN-1Q9	Human B-cell leukemia/lymphoma 2 (bcl-	1744	286G>A	A96T

SD-144146.1

M14221	M14221	161565	GEN-QM	proteinase mRNA, complete cds	1557	1363G>C	3
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1585	1391C>A	3
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1630	1436T>C	3
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1668	1474T>G	3
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1712	1518C>G	3
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1898	1704A>G	3
ARG1	M14502	207800	GEN- 1RE	Human liver arginase mRNA, complete cds	800	744C>T	S
ABL1	M14752	189980	GEN- 1S7	Human c-abl gene, complete cds	2233	1869G>A	S
ABL1	M14752	189980	GEN- 1S7	Human c-abl gene, complete cds	3826	3462A>G	3
M14758	M14758	171050	GEN- 1S6	P glycoprotein 1	978	554- 555TT>GA>G	V185G
M14758	M14758	171050	GEN- 1S6	P glycoprotein 1	978	554- 555TT>TT	S
M14758	M14758	171050	GEN- 1S6	P glycoprotein 1	1623	1199G>A	S400N
M14758	M14758	171050	GEN- 1S6	P glycoprotein 1	3101	2677G>A	A893T
M14758	M14758	171050	GEN- 1S6	P glycoprotein 1	3101	2677G>T	A893S
M14758	M14758	171050	GEN- 1S6	P glycoprotein 1	3859	3435C>T	S
M14758	M14758	171050	GEN- 1S6	P glycoprotein 1	4460	4036A>G	3

NGFR	M14764	162010	GEN-1S8	Human nerve growth factor receptor mRNA, complete cds	2716	2603C>T	3
NGFR	M14764	162010	GEN-1S8	Human nerve growth factor receptor mRNA, complete cds	2729	2616C>T	3
NGFR	M14764	162010	GEN-1S8	Human nerve growth factor receptor mRNA, complete cds	2912	2799G>A	3
NGFR	M14764	162010	GEN-1S8	Human nerve growth factor receptor mRNA, complete cds	3252	3139C>G	3
M15395	M15395	600065	GEN-U	Leukocyte integrin beta-2	890	818G>A	G273E
M15395	M15395	600065	GEN-U	Leukocyte integrin beta-2	978	906A>G	S
M15395	M15395	600065	GEN-U	Leukocyte integrin beta-2	1173	1101C>A	S
M15395	M15395	600065	GEN-U	Leukocyte integrin beta-2	1395	1323T>C	S
M15395	M15395	600065	GEN-U	Leukocyte integrin beta-2	1614	1542C>T	S
M15395	M15395	600065	GEN-U	Leukocyte integrin beta-2	1965	1893C>T	S
M15395	M15395	600065	GEN-U	Leukocyte integrin beta-2	2505	2433G>A	3
M15395	M15395	600065	GEN-U	Leukocyte integrin beta-2	2505	2433G>A	3
M15395	M15395	600065	GEN-U	Leukocyte integrin beta-2	2528	2456C>A	3
M15395	M15395	600065	GEN-U	Leukocyte integrin beta-2	2528	2456C>A	3
M15395	M15395	600065	GEN-U	Leukocyte integrin beta-2	2553	2481G>C	3
PCNA	M15796	176740	GEN-1UE	Human cyclin protein gene, complete cds	1063	945C>G	3
M15872	M15872	138360	GEN-QS	Human glutathione S-transferase 2 (GST) mRNA, complete cds	16	(-40)G>A	5
M15872	M15872	138360	GEN-QS	Human glutathione S-transferase 2 (GST) mRNA, complete cds	54	(-2)T>C	5
M15872	M15872	138360	GEN-QS	Human glutathione S-transferase 2 (GST) mRNA, complete cds	84	29T>C	F10S
M15872	M15872	138360	GEN-QS	Human glutathione S-transferase 2 (GST) mRNA, complete cds	111	56C>T	T19I
M15872	M15872	138360	GEN-QS	Human glutathione S-transferase 2 (GST) mRNA, complete cds	170	115G>T	F

M15872	M15872	138360	GEN-QS	mRNA, complete cds	321	266G>A	R89K
				Human glutathione S-transferase 2 (GST)			
M15872	M15872	138360	GEN-QS	mRNA, complete cds	376	321C>T	S
				Human glutathione S-transferase 2 (GST)			
M15872	M15872	138360	GEN-QS	mRNA, complete cds	430	375G>A	S
				Human glutathione S-transferase 2 (GST)			
M15872	M15872	138360	GEN-QS	mRNA, complete cds	622	567C>T	S
				Human glutathione S-transferase 2 (GST)			
M15872	M15872	138360	GEN-QS	mRNA, complete cds	684	629A>C	E210A
				Human glutathione S-transferase 2 (GST)			
M15872	M15872	138360	GEN-QS	mRNA, complete cds	701	646G>T	A216S
				Human glutathione S-transferase 2 (GST)			
M15990	M15990	164880	GEN-1UR	mRNA, complete cds	3403	3196G>A	3
				Human c-yes-1 mRNA			
M15990	M15990	164880	GEN-1UR	Human c-yes-1 mRNA	3864	3657G>A	3
				Human c-yes-1 mRNA			
M15990	M15990	164880	GEN-1UR	Human c-yes-1 mRNA	3969	3762A>C	3
				Human c-yes-1 mRNA			
M15990	M15990	164880	GEN-1UR	Human c-yes-1 mRNA	4148	3941T>C	3
				Human c-yes-1 mRNA			
M16650	M16650	165640	GEN-EH	Ornithine decarboxylase 1	1330	1243G>C	E415Q
				Ornithine decarboxylase 1			
M16650	M16650	165640	GEN-EH	Ornithine decarboxylase 1	1356	1269C>T	S
				Ornithine decarboxylase 1			
M20132	M20132	313700	GEN-38	Androgen receptor (dihydrotestosterone receptor)	995	633G>A	S
				Androgen receptor (dihydrotestosterone receptor)			
M20132	M20132	313700	GEN-38	Androgen receptor (dihydrotestosterone receptor)	1385	1023T>C	S
				Androgen receptor (dihydrotestosterone receptor)			
M20132	M20132	313700	GEN-38	Androgen receptor (dihydrotestosterone receptor)	1786	1424G>A	G475E
				Androgen receptor (dihydrotestosterone receptor)			
M20137	M20137	147740	GEN-CCJ	Human interleukin 3 (IL-3) mRNA, complete cds, clone pcD-SR-alpha	132	79C>T	P27S

M20566	M20566	147880	GEN-3A	Interleukin 6A	3058	2621A>T	3
M21154	M21154	180980	GEN-EM	S-adenosylmethionine decarboxylase 1	1050	802A>G	I268V
M21154	M21154	180980	GEN-EM	S-adenosylmethionine decarboxylase 1	1139	891T>G	S
M24857	M24857	180190	GEN-80	Retinoic acid receptor, gamma 1	1694	1280C>T	S427L
SCYA3	M25315	601395	GEN-29M	Homo sapiens (clone pAT 464) potential lymphokine/cytokine mRNA, complete cds	32	(-52)T>C	5
SCYA3	M25315	601395	GEN-29M	Homo sapiens (clone pAT 464) potential lymphokine/cytokine mRNA, complete cds	67	(-17)G>A	5
SCYA3	M25315	601395	GEN-29M	Homo sapiens (clone pAT 464) potential lymphokine/cytokine mRNA, complete cds	110	27T>C	S
SCYA3	M25315	601395	GEN-29M	Homo sapiens (clone pAT 464) potential lymphokine/cytokine mRNA, complete cds	153	70T>C	S24P
SCYA3	M25315	601395	GEN-29M	Homo sapiens (clone pAT 464) potential lymphokine/cytokine mRNA, complete cds	203	120G>A	S
SCYA3	M25315	601395	GEN-29M	Homo sapiens (clone pAT 464) potential lymphokine/cytokine mRNA, complete cds	263	180C>T	S
SCYA3	M25315	601395	GEN-29M	Homo sapiens (clone pAT 464) potential lymphokine/cytokine mRNA, complete cds	264	181G>A	G61S
SCYA3	M25315	601395	GEN-29M	Homo sapiens (clone pAT 464) potential lymphokine/cytokine mRNA, complete cds	285	202C>A	S
SCYA3	M25315	601395	GEN-29M	Homo sapiens (clone pAT 464) potential lymphokine/cytokine mRNA, complete cds	288	205A>G	S69G

SCYA3	M25315	601395	GEN- 29M	lymphokine/cytokine mRNA, complete cds Homo sapiens (clone pAT 464) potential	291	208C>G	R70G
SCYA3	M25315	601395	GEN- 29M	lymphokine/cytokine mRNA, complete cds Homo sapiens (clone pAT 464) potential	335	252T>C	S
SCYA3	M25315	601395	GEN- 29M	lymphokine/cytokine mRNA, complete cds Homo sapiens (clone pAT 464) potential	341	258C>T	S
SCYA3	M25315	601395	GEN- 29M	lymphokine/cytokine mRNA, complete cds Homo sapiens (clone pAT 464) potential	395	312G>A	3
SCYA3	M25315	601395	GEN- 29M	lymphokine/cytokine mRNA, complete cds Homo sapiens (clone pAT 464) potential	452	369C>T	3
SCYA3	M25315	601395	GEN- 29M	lymphokine/cytokine mRNA, complete cds Homo sapiens (clone pAT 464) potential	479	396G>A	3
SCYA3	M25315	601395	GEN- 29M	lymphokine/cytokine mRNA, complete cds Homo sapiens (clone pAT 464) potential	549	466G>A	3
SCYA3	M25315	601395	GEN- 29M	lymphokine/cytokine mRNA, complete cds Homo sapiens (clone pAT 464) potential	561	478C>T	3
SCYA3	M25315	601395	GEN- 29M	lymphokine/cytokine mRNA, complete cds Homo sapiens (clone pAT 464) potential	617	534C>G	3
SCYA3	M25315	601395	GEN- 29M	lymphokine/cytokine mRNA, complete cds Homo sapiens (clone pAT 464) potential	660	577A>G	3

M25753	M25753	123836	GEN-ET	mRNA, complete cds	167	168C>T	3
M25753	M25753	123836	GEN-ET	Cyclin B1	1055	1056G>A	3
M26383	M26383	146930	GEN-3E	Interleukin 8	259	185C>G	A62G
M26383	M26383	146930	GEN-3E	Interleukin 8	1237	1163A>T	3
M26383	M26383	146930	GEN-3E	Interleukin 8	1281	1207A>G	3
M27396	M27396	108370	GEN-EX	Asparagine Synthase	807	629T>A	V210E
M27396	M27396	108370	GEN-EX	Asparagine Synthase	1387	1209C>G	S
M27492	M27492	147810	GEN-3F	INTERLEUKIN 1 RECEPTOR, TYPE I	4686	4604T>G	3
M29696	M29696	146661	GEN-3H	PRECURSOR			
M31145	M31145	146730	GEN-3J	Interleukin 7 receptor	1088	1066G>A	V356I
M31145	M31145	146730	GEN-3J	Insulin-like growth factor binding protein 1 precursor	923	759A>G	I253M
M31145	M31145	146730	GEN-3J	Insulin-like growth factor binding protein 1 precursor	1048	884T>C	3
M31145	M31145	146730	GEN-3J	Insulin-like growth factor binding protein 1 precursor	1260	1096C>G	3
M31159	M31159	146732	GEN- 2GD	Human growth hormone- dependent insulin-like growth factor-binding protein mRNA, complete cds	204	95G>C	G32A
M31159	M31159	146732	GEN- 2GD	Human growth hormone- dependent insulin-like growth factor-binding protein mRNA, complete cds	2178	2069A>T	3
M32313	M32313	184753	GEN-5Y	Steroid 5 alpha reductase 1	1271	1241C>T	3
M32313	M32313	184753	GEN-5Y	Steroid 5 alpha reductase 1	1344	1314G>A	3
M32313	M32313	184753	GEN-5Y	Steroid 5 alpha reductase 1	1489	1459G>A	3
M32313	M32313	184753	GEN-5Y	Steroid 5 alpha reductase 1	1780	1750T>C	3
M32315	M32315	191191	GEN-3M	Tumor necrosis factor receptor 2 (75kD)	676	587T>G	M196R
M32315	M32315	191191	GEN-3M	Tumor necrosis factor receptor 2 (75kD)	1176	1087G>A	A363T

M32315	M32315	191191	GEN-3M	Tumor necrosis factor receptor 2 (75kD)	1668	1579G>T	3
M32315	M32315	191191	GEN-3M	Tumor necrosis factor receptor 2 (75kD)	2898	2809G>A	3
M32315	M32315	191191	GEN-3M	Tumor necrosis factor receptor 2 (75kD)	3671	3582G>A	3
VEGF	M32977	192240	GEN-2JF	Human heparin-binding vascular endothelial growth factor (VEGF) mRNA, complete cds	50	(-7)C>T	5
VEGF	M32977	192240	GEN-2JF	Human heparin-binding vascular endothelial growth factor (VEGF) mRNA, complete cds	92	36C>T	S
RB1	M33647	180200	GEN-2K1	Human retinoblastoma associated (RB1) mRNA, complete cds	1105	1102G>A	V368I
M35011	M35011	147561	GEN-2LV	Human integrin beta-5 subunit mRNA, complete cds	1448	1419C>T	S
M35011	M35011	147561	GEN-2LV	Human integrin beta-5 subunit mRNA, complete cds	2778	2749A>C	3
M35011	M35011	147561	GEN-2LV	Human integrin beta-5 subunit mRNA, complete cds	2904	2875T>C	3
M35011	M35011	147561	GEN-2LV	Human integrin beta-5 subunit mRNA, complete cds	3077	3048G>A	3
M35011	M35011	147561	GEN-2LV	Human integrin beta-5 subunit mRNA, complete cds	3095	3066T>A	3
MET	M35074	164860	GEN-2LU	Human met oncogene mRNA, 3 end	60	60C>T	S
MET	M35074	164860	GEN-2LU	Human met oncogene mRNA, 3 end	294	294G>A	S
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	53	35T>C	V12A
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	900	882T>C	S
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	1161	1143C>A	S
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	1161	1143C>A	S

M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	1551	1533G>A	S
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	1551	1533G>A	S
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	1563	1545G>A	S
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	1563	1545G>A	S
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	2226	2208C>T	S
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	2426	2408G>C	3
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	3056	3038C>T	3
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	3098	3080A>G	3
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	3403	3385A>T	3
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	3927	3909C>T	3
M37825	M37825	165190	GEN-2OM	Human fibroblast growth factor-5 (FGF-5) mRNA, complete cds	787	648T>G	S
M54968	M54968	190070	GEN-35G	Human K-ras oncogene protein mRNA, complete cds	711	519T>C	S
M54968	M54968	190070	GEN-35G	Human K-ras oncogene protein mRNA, complete cds	936	744G>T	3
M54968	M54968	190070	GEN-35G	Human K-ras oncogene protein mRNA, complete cds	1270	1078T>C	3
M54968	M54968	190070	GEN-35G	Human K-ras oncogene protein mRNA, complete cds	3268	3076T>G	3
M54968	M54968	190070	GEN-35G	Human K-ras oncogene protein mRNA, complete cds	4529	4337A>C	3
M54968	M54968	190070	GEN-35G	Human K-ras oncogene protein mRNA, complete cds	4555	4363A>G	3
M54968	M54968	190070	GEN-35G	Human K-ras oncogene protein mRNA, complete cds	4672	4480A>C	3
CSNK2A1	M55265	115440	GEN-35Y	Human casein kinase II alpha subunit mRNA, complete cds	193	45T>C	S
CSNK2A1	M55265	115440	GEN-35Y	Human casein kinase II alpha subunit mRNA, complete cds	1007	859A>C	S287R

CSNK2A1	M55265	115440	GEN-35Y	Human casein kinase II alpha subunit mRNA, complete cds	1180	1032G>A	S
CSNK2A1	M55265	115440	GEN-35Y	Human casein kinase II alpha subunit mRNA, complete cds	1199	1051A>G	M351V
CSNK2A2	M55268	115442	GEN-35X	Human casein kinase II alpha subunit mRNA, complete cds	1532	1369C>A	3
M59979	M59979	176805	GEN-Z	Cyclooxygenase 1 COX1	644	639C>A	S
M59979	M59979	176805	GEN-Z	Cyclooxygenase 1 COX1	1892	1887C>A	3
M59979	M59979	176805	GEN-Z	Cyclooxygenase 1 COX1	2030	2025G>A	3
M60761	M60761	156569	GEN-FL	O-6-methylguanine-DNA methyltransferase	174	159C>T	S
M60761	M60761	156569	GEN-FL	O-6-methylguanine-DNA methyltransferase	174	159C>T	S
M60761	M60761	156569	GEN-FL	O-6-methylguanine-DNA methyltransferase	174	159C>T	S
M60761	M60761	156569	GEN-FL	O-6-methylguanine-DNA methyltransferase	210	195G>C	W65C
M60761	M60761	156569	GEN-FL	O-6-methylguanine-DNA methyltransferase	264	249A>T	S
M60761	M60761	156569	GEN-FL	O-6-methylguanine-DNA methyltransferase	265	250C>T	L84F
M60761	M60761	156569	GEN-FL	O-6-methylguanine-DNA methyltransferase	265	250C>T	L84F
M60761	M60761	156569	GEN-FL	O-6-methylguanine-DNA methyltransferase	442	427A>G	I143V
M60761	M60761	156569	GEN-FL	O-6-methylguanine-DNA methyltransferase	442	427A>G	I143V
M60761	M60761	156569	GEN-FL	O-6-methylguanine-DNA methyltransferase	493	478G>A	G160R
M60761	M60761	156569	GEN-FL	O-6-methylguanine-DNA methyltransferase	548	533A>G	K178R
M60761	M60761	156569	GEN-FL	O-6-methylguanine-DNA methyltransferase	582	567G>A	S
FGF7	M60828	148180	GEN-3BE	Human keratinocyte growth factor mRNA, complete cds	323	(-123)G>C	5
FGF7	M60828	148180	GEN-3BE	Human keratinocyte growth factor mRNA, complete cds	1180	735T>C	3

SD-144146.1

FGF7	M60828	148180	GEN-3BE	complete cds Human keratinocyte growth factor mRNA,	1201	756A>G	3
FGF7	M60828	148180	GEN-3BE	complete cds Human keratinocyte growth factor mRNA,	1216	771A>G	3
FGF7	M60828	148180	GEN-3BE	complete cds Human keratinocyte growth factor mRNA,	1218	773G>C	3
FGF7	M60828	148180	GEN-3BE	complete cds Human keratinocyte growth factor mRNA,	1266	821A>C	3
FGF7	M60828	148180	GEN-3BE	complete cds Human keratinocyte growth factor mRNA,	1306	861C>T	3
FGF7	M60828	148180	GEN-3BE	complete cds Human keratinocyte growth factor mRNA,	1654	1209A>T	3
FGF7	M60828	148180	GEN-3BE	complete cds Human keratinocyte growth factor mRNA,	1657	1212T>C	3
FGF7	M60828	148180	GEN-3BE	complete cds Human keratinocyte growth factor mRNA,	1799	1354A>T	3
FGF7	M60828	148180	GEN-3BE	complete cds Human keratinocyte growth factor mRNA,	1801	1356C>T	3
FGF7	M60828	148180	GEN-3BE	complete cds Human keratinocyte growth factor mRNA,	1867	1422A>G	3
FGF7	M60828	148180	GEN-3BE	complete cds Human keratinocyte growth factor mRNA,	1945	1500C>A	3
FGF7	M60828	148180	GEN-3BE	complete cds Human keratinocyte growth factor mRNA,	1973	1528G>A	3
FGF7	M60828	148180	GEN-3BE	complete cds Human keratinocyte growth factor mRNA,	2167	1722G>A	3
FGF7	M60828	148180	GEN-3BE	complete cds Human keratinocyte growth factor mRNA,	2186	1741A>G	3

FGF7	M60828	148180	3BE	growth factor mRNA, complete cds	2302	1857T>A	3
			GEN-3BE	Human keratinocyte growth factor mRNA, complete cds	2328	1883G>A	3
FGF7	M60828	148180	GEN-3BE	Human keratinocyte growth factor mRNA, complete cds	693	669A>G	S
M61764	M61764	191135	GEN-FO	Tubulin, gamma polypeptide	723	699T>C	S
M61764	M61764	191135	GEN-FO	Tubulin, gamma polypeptide	849	825T>G	S
M61764	M61764	191135	GEN-FO	Tubulin, gamma polypeptide	858	834G>A	S
M61764	M61764	191135	GEN-FO	Tubulin, gamma polypeptide	1033	1009T>C	S
M61764	M61764	191135	GEN-FO	Tubulin, gamma polypeptide	1053	1029C>G	S
M61764	M61764	191135	GEN-FO	Tubulin, gamma polypeptide	1131	1107G>A	S
M61764	M61764	191135	GEN-FO	Tubulin, gamma polypeptide	1188	1164C>T	S
IGFBP4	M62403	146733	GEN-3CJ	Human insulin-like growth factor binding protein 4 (IGFBP4) mRNA, complete cds	859	776G>A	S
IGFBP4	M62403	146733	GEN-3CJ	Human insulin-like growth factor binding protein 4 (IGFBP4) mRNA, complete cds	1403	1320G>T	3
IGFBP4	M62403	146733	GEN-3CJ	Human insulin-like growth factor binding protein 4 (IGFBP4) mRNA, complete cds	1443	1360G>A	3
IGFBP4	M62403	146733	GEN-3CJ	Human insulin-like growth factor binding protein 4 (IGFBP4) mRNA, complete cds	1446	1363G>A	3
IGFBP4	M62403	146733	GEN-3CJ	Human insulin-like growth factor binding protein 4 (IGFBP4) mRNA, complete cds	1485	1402A>T	3

M62782	M62782	146734	GEN-3CU	factor binding protein 4 (IGFBP4) mRNA, complete cds	908	852C>T	3
M62982	M62982	152391	GEN-12	Homo sapiens insulin-like growth factor binding protein 5 (IGFBP-5) mRNA, complete cds	1018	965G>A	S322N
M62982	M62982	152391	GEN-12	Lipoxygenases: 12-lipoxygenase (platelet)	1145	1092T>G	S
AKT1	M63167	164730	GEN-3D7	Lipoxygenases: 12-lipoxygenase (platelet)	934	736T>G	S246A
AKT1	M63167	164730	GEN-3D7	Human rac protein kinase alpha mRNA, complete cds	1964	1766G>A	3
M63509	M63509	138380	GEN-9G	Human rac protein kinase alpha mRNA, complete cds	644	628A>T	T210S
FGFR3	M64347	134934	GEN-3EX	Glutathione S-transferase M2 (muscle)	3108	3108C>A	3
FGFR3	M64347	134934	GEN-3EX	Human novel growth factor receptor mRNA, 3 cds	3715	3715G>A	3
M68892	M68892	147559	GEN-15	Human novel growth factor receptor mRNA, 3 cds	1327	1176C>T	S
IGFBP6	M69054	146735	GEN-3J0	Leukocyte integrin beta-7	751	751A>C	3
IGFBP6	M69054	146735	GEN-3J0	Human insulin-like growth factor binding protein 6 (IGFBP6) mRNA, complete mature peptide	835	835A>C	3
IGFBP6	M69054	146735	GEN-3J0	Human insulin-like growth factor binding protein 6 (IGFBP6) mRNA, complete mature peptide	850	850G>A	3
M73554	M73554	168461	GEN-FY	Human insulin-like growth factor binding protein 6 (IGFBP6) mRNA, complete mature peptide	864	723G>A	S
M73554	M73554	168461	GEN-FY	Cyclin D1	1094	953A>C	3
M73554	M73554	168461	GEN-FY	Cyclin D1	1094	953A>C	3
M73554	M73554	168461	GEN-FY	Cyclin D1	1367	1226T>G	3
M73554	M73554	168461	GEN-FY	Cyclin D1	3899	3758T>G	3
M73554	M73554	168461	GEN-FY	Cyclin D1	4013	3872A>G	3

SRD5A2	M74047	264600	GEN- CDC	Human steroid 5-alpha-reductase 2 (SRD5A2) mRNA, complete cds	2379	2352A>G	3
M74091	M74091	123838	GEN-FZ	G1/S-SPECIFIC CYCLIN C	41	42C>G	3
CCNE	M74093	123837	GEN- 3MX	Human cyclin mRNA	1195	1196C>T	3
CCNE	M74093	123837	GEN- 3MX	Human cyclin mRNA	1641	1642C>A	3
M74782	M74782	308385	GEN-64	Interleukin 3 receptor, alpha (low affinity)	1396	1250C>T	3
MPG	M74905	156565	GEN- 3NL	Human 3-alkyladenine DNA glycosylase (HAAG) mRNA, complete cds	254	108C>T	S
MPG	M74905	156565	GEN- 3NL	Human 3-alkyladenine DNA glycosylase (HAAG) mRNA, complete cds	350	204G>A	S
MPG	M74905	156565	GEN- 3NL	Human 3-alkyladenine DNA glycosylase (HAAG) mRNA, complete cds	413	267G>A	S
MPG	M74905	156565	GEN- 3NL	Human 3-alkyladenine DNA glycosylase (HAAG) mRNA, complete cds	416	270C>T	S
MPG	M74905	156565	GEN- 3NL	Human 3-alkyladenine DNA glycosylase (HAAG) mRNA, complete cds	546	400C>G	P134A
MPG	M74905	156565	GEN- 3NL	Human 3-alkyladenine DNA glycosylase (HAAG) mRNA, complete cds	743	597C>T	S
M80646	M80646	274180	GEN-40	Thromboxane synthase	756	585G>C	S
M80646	M80646	274180	GEN-40	Thromboxane synthase	1240	1069C>G	L357V
M81695	M81695	151510	GEN-17	Leukocyte integrin alpha-x	1834	1770G>C	S
M81695	M81695	151510	GEN-17	Leukocyte integrin alpha-x	3282	3218C>T	T1073M
M81695	M81695	151510	GEN-17	Leukocyte integrin alpha-x	4213	4149C>G	3
M84747	M84747	300007	GEN-45	Interleukin 9 receptor	1273	1094G>A	R365H
TGFBR2	M85079	190182	GEN- 3ZS	Human TGF-beta type II receptor mRNA, complete cds	2045	1710A>C	3
M90100	M90100	600262	GEN-1A	Cyclooxygenase 2 COX2	2159	2062G>C	3
M90100	M90100	600262	GEN-1A	Cyclooxygenase 2 COX2	2186	2089- 2094ATATTA	3

M90100	M90100	600262	GEN-1A	Cyclooxygenase 2 COX2	2186	>ATATTA 2094delATAT	3
M90100	M90100	600262	GEN-1A	Cyclooxygenase 2 COX2	2230	TA 2133A>G	3
M90100	M90100	600262	GEN-1A	Cyclooxygenase 2 COX2	2339	2242T>C	3
M90100	M90100	600262	GEN-1A	Cyclooxygenase 2 COX2	2409	2312G>A	3
M90100	M90100	600262	GEN-1A	Cyclooxygenase 2 COX2	2726	2629C>T	3
M90100	M90100	600262	GEN-1A	Cyclooxygenase 2 COX2	2983	2886C>T	3
M90814	M90814	123834	GEN-GK	Cyclin D3	1648	1548G>A	3
IL8RB	M94582	146928	GEN-49G	Interleukin 8 receptor	838	786T>C	S
IL8RB	M94582	146928	GEN-49G	Interleukin 8 receptor	1262	1210C>T	3
IL8RB	M94582	146928	GEN-49G	Interleukin 8 receptor	1494	1442A>G	3
BRAF	M95712	164757	GEN-4AD	Human B-raf mRNA, complete cds	284	223T>G	S75A
M96234	M96234	138333	GEN-9J	Glutathione S-transferase M4	797	534T>C	S
M96652	M96652	147851	GEN-65	Interleukin 5 receptor alpha	883	634T>G	S212A
M98045	M98045	136510	GEN-4C3	Homo sapiens folypolyglutamate synthetase mRNA, complete cds	802	732C>T	S
M98045	M98045	136510	GEN-4C3	Homo sapiens folypolyglutamate synthetase mRNA, complete cds	1747	1677G>T	3
M98045	M98045	136510	GEN-4C3	Homo sapiens folypolyglutamate synthetase mRNA, complete cds	1900	1830T>C	3
M98045	M98045	136510	GEN-4C3	Homo sapiens folypolyglutamate synthetase mRNA, complete cds	1900	1830T>C	3
M98045	M98045	136510	GEN-4C3	Homo sapiens folypolyglutamate synthetase mRNA, complete cds	1912	1842G>A	3

M98045	M98045	136510	GEN-4C3	complete cds Homo sapiens folypolyglutamate synthetase mRNA,	1995	1925C>G	3
M98539	M98539	176803	GEN-SW	complete cds prostaglandin D2 synthase gene	157	158C>A	3
S72487	S72487	131222	GEN-3LD	orf1 5 to PD- ECGF/TP...orf2 5 to PD- ECGF/TP [human, epidermoid carcinoma cell line A431, mRNA, 3 genes, 1718 nt]	183	19G>A	D7N
S72487	S72487	131222	GEN-3LD	orf1 5 to PD- ECGF/TP...orf2 5 to PD- ECGF/TP [human, epidermoid carcinoma cell line A431, mRNA, 3 genes, 1718 nt]	483	319C>T	3
S72487	S72487	131222	GEN-3LD	orf1 5 to PD- ECGF/TP...orf2 5 to PD- ECGF/TP [human, epidermoid carcinoma cell line A431, mRNA, 3 genes, 1718 nt]	601	437G>C	3
S72487	S72487	131222	GEN-3LD	orf1 5 to PD- ECGF/TP...orf2 5 to PD- ECGF/TP [human, epidermoid carcinoma cell line A431, mRNA, 3 genes, 1718 nt]	1299	1135G>A	3
PDCD2	S78085	600866	GEN-3QQ	PDCD2=programmed cell death-2/Rp8 homolog [human, fetal lung, mRNA, 1718 nt]	1180	1151G>A	3
U00672	U00672	146933	GEN-4A	Interleukin 10 receptor	3377	3316A>C	3
U00672	U00672	146933	GEN-4A	Interleukin 10 receptor	3524	3463A>G	3
U03858	U03858	600007	GEN-MDM	Fms-related tyrosine kinase 3 ligand	683	600C>T	S
U03858	U03858	600007	GEN-MDM	Fms-related tyrosine kinase 3 ligand	1016	933T>C	3

PI5	U04313	154790	GEN-14A	Human maspin mRNA, complete cds	2496	2421G>C	3
NTRK3	U05012	191316	GEN-16V	Human receptor tyrosine kinase TrkC (NTRK3) mRNA, complete cds	364	209G>A	S70N
NTRK3	U05012	191316	GEN-16V	Human receptor tyrosine kinase TrkC (NTRK3) mRNA, complete cds	728	573C>T	S
NTRK3	U05012	191316	GEN-16V	Human receptor tyrosine kinase TrkC (NTRK3) mRNA, complete cds	1613	1458C>T	S
NTRK3	U05012	191316	GEN-16V	Human receptor tyrosine kinase TrkC (NTRK3) mRNA, complete cds	1643	1488G>C	S
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	38	15C>T	S
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	282	259A>T	S87C
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	350	327C>T	S
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	365	342T>C	S
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	464	441G>A	S
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	474	451A>G	M151V
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	532	509A>G	H170R
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	538	515T>A	L172Q
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	689	666T>C	S

SD-144146.1

DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	806	783G>A	S
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	872	849G>T	S
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	952	929T>G	I310S
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	1020	997G>A	3
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	1035	1012G>A	3
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	1112	1089C>T	3
U05875	U05875	147569	GEN-18J	Human clone pSK1 interferon gamma receptor accessory factor-1 (AF-1) mRNA, complete cds	2047	1399C>G	3
U05875	U05875	147569	GEN-18J	Human clone pSK1 interferon gamma receptor accessory factor-1 (AF-1) mRNA, complete cds	2087	1439T>C	3
XDH	U06117	278300	GEN-194	Human xanthine dehydrogenase (XDH) mRNA, complete cds	3951	3888C>G	S
U09178	U09178	274270	GEN-HA	Dihydropyrimidine Dehydrogenase	166	85T>C	C29R
U09178	U09178	274270	GEN-HA	Dihydropyrimidine Dehydrogenase	166	85T>C	C29R
U09178	U09178	274270	GEN-HA	Dihydropyrimidine Dehydrogenase	577	496A>G	M166V
U09178	U09178	274270	GEN-HA	Dihydropyrimidine Dehydrogenase	638	557A>G	Y186C
U09178	U09178	274270	GEN-HA	Dihydropyrimidine Dehydrogenase	1708	1627A>G	I543V
U09178	U09178	274270	GEN-HA	Dihydropyrimidine Dehydrogenase	3432	3351T>C	3

U09178	U09178	274270	GEN-HA	Dihydropyrimidine Dehydrogenase	3730	3649G>A	3
U09178	U09178	274270	GEN-HA	Dihydropyrimidine Dehydrogenase	3925	3844A>G	3
U09178	U09178	274270	GEN-HA	Dihydropyrimidine Dehydrogenase	3937	3856T>C	3
U09579	U09579	116899	GEN- 1GZ	Human melanoma differentiation associated (mda-6) mRNA, complete cds	609	515C>T	3
U09579	U09579	116899	GEN- 1GZ	Human melanoma differentiation associated (mda-6) mRNA, complete cds	1875	1781G>A	3
U09579	U09579	116899	GEN- 1GZ	Human melanoma differentiation associated (mda-6) mRNA, complete cds	1877	1783C>G	3
U09759	U09759	602896	GEN- 1HA	Human protein kinase (JNK2) mRNA, complete cds	303	152A>G	N51S
U09759	U09759	602896	GEN- 1HA	Human protein kinase (JNK2) mRNA, complete cds	1079	928A>G	I310V
U09759	U09759	602896	GEN- 1HA	Human protein kinase (JNK2) mRNA, complete cds	1280	1129C>T	P377S
U09759	U09759	602896	GEN- 1HA	Human protein kinase (JNK2) mRNA, complete cds	1559	1408C>T	3
U09806	U09806	None	GEN- 4FZ	Human methylenetetrahydrofolate reductase mRNA, partial cds	120	120T>C	S
U09806	U09806	None	GEN- 4FZ	Human methylenetetrahydrofolate reductase mRNA, partial cds	473	473G>A	R158Q
U09806	U09806	None	GEN- 4FZ	Human methylenetetrahydrofolate reductase mRNA, partial cds	550	550C>T	F

SD-144146.1

U09806	U09806	None	GEN-4FZ	cds Human methylenetetrahydrofolate reductase mRNA, partial	668	668C>T	A223V
U09806	U09806	None	GEN-4FZ	cds Human methylenetetrahydrofolate reductase mRNA, partial	1059	1059T>C	S
U09806	U09806	None	GEN-4FZ	cds Human methylenetetrahydrofolate reductase mRNA, partial	1289	1289C>A	E430A
U09806	U09806	None	GEN-4FZ	cds Human methylenetetrahydrofolate reductase mRNA, partial	1308	1308T>C	3
U09850	U09850	603433	GEN-1HD	cds Human zinc finger protein (ZNF143) mRNA, complete	1383	1346G>A	G449D
U09850	U09850	603433	GEN-1HD	cds Human zinc finger protein (ZNF143) mRNA, complete	2443	2406C>T	3
U09850	U09850	603433	GEN-1HD	cds Human zinc finger protein (ZNF143) mRNA, complete	2950	2913A>G	3
U09850	U09850	603433	GEN-1HD	cds Human zinc finger protein (ZNF143) mRNA, complete	3001	2964G>A	3
U09850	U09850	603433	GEN-1HD	cds Human zinc finger protein (ZNF143) mRNA, complete	3120	3083T>C	3
U09850	U09850	603433	GEN-1HD	cds Human zinc finger protein (ZNF143) mRNA, complete	3745	3708T>C	3
THPO	U11025	600044	GEN-1JW	cds Human megakaryocyte growth and development factor (MGDF) mRNA, complete cds	76	41T>C	L14P
THPO	U11025	600044	GEN-1JW	cds Human megakaryocyte growth and development factor (MGDF) mRNA, complete cds	172	137G>A	R46K

THPO	U11025	600044	GEN-1JW	factor (MGDF) mRNA, complete cds Human megakaryocyte growth and development factor (MGDF) mRNA, complete cds	382	347G>A	G116E
THPO	U11025	600044	GEN-1JW	Human megakaryocyte growth and development factor (MGDF) mRNA, complete cds	674	639T>A	S
THPO	U11025	600044	GEN-1JW	Human megakaryocyte growth and development factor (MGDF) mRNA, complete cds	1132	1097G>A	3
U11791	U11791	601953	GEN-HF	Cyclin H	823	763A>G	M255V
TPMT	U12387	187680	GEN-1LY	Human thiopurine methyltransferase (TPMT) mRNA, complete cds	536	460G>A	A154T
TPMT	U12387	187680	GEN-1LY	Human thiopurine methyltransferase (TPMT) mRNA, complete cds	795	719A>G	Y240C
TPMT	U12387	187680	GEN-1LY	Human thiopurine methyltransferase (TPMT) mRNA, complete cds	1085	1009T>C	3
TPMT	U12387	187680	GEN-1LY	Human thiopurine methyltransferase (TPMT) mRNA, complete cds	1336	1260C>T	3
TPMT	U12387	187680	GEN-1LY	Human thiopurine methyltransferase (TPMT) mRNA, complete cds	1373	1297G>A	3
U13737	U13737	600636	GEN-1PC	Human cysteine protease CPP32 isoform alpha mRNA, complete cds	2356	2132A>C	3
U13737	U13737	600636	GEN-1PC	Human cysteine protease CPP32 isoform alpha mRNA, complete cds	2535	2311C>T	3
BRCA1	U14680	113705	GEN-1S1	Human breast and ovarian cancer susceptibility (BRCA1) mRNA, complete cds	4427	4308T>C	S
U19251	U19251	600355	GEN-221	Homo sapiens neuronal	2223	1932T>G	F644L

U19251	U19251	600355	GEN-221	apoptosis inhibitory protein mRNA, complete cds	3046	2755C>T	P919S
U19251	U19251	600355	GEN-221	Homo sapiens neuronal apoptosis inhibitory protein mRNA, complete cds	5503	5212A>G	3
U19251	U19251	600355	GEN-221	apoptosis inhibitory protein mRNA, complete cds	5634	5343A>G	3
U19251	U19251	600355	GEN-221	Homo sapiens neuronal apoptosis inhibitory protein mRNA, complete cds	5644	5353A>G	3
U19487	U19487	176804	GEN-41	Homo sapiens neuronal apoptosis inhibitory protein mRNA, complete cds	231	75A>T	S
U19720	U19720	600424	GEN-I1	PROSTAGLANDIN E2 RECEPTOR, EP2 SUBTYPE	53	(-43)T>C	5
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	175	80G>A	R27H
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	175	80G>A	R27H
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	341	246C>G	S
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	791	696C>T	S
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	1067	972G>A	S
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	2100	2005^2006ins G	F
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	2582	2487T>G	3
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	2582	2487T>G	3
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	2617	2522C>T	3
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	2617	2522C>T	3
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	2652	2557T>C	3

U19775	U19775	600289	GEN-22C	Human MAP kinase Mxi2 (MXI2) mRNA, complete cds	731	688G>A	D230N
U20536	U20536	601532	GEN-23K	Human cysteine protease Mch2 isoform alpha (Mch2) mRNA, complete cds	982	904C>T	3
U20536	U20536	601532	GEN-23K	Human cysteine protease Mch2 isoform alpha (Mch2) mRNA, complete cds	1117	1039G>A	3
U20536	U20536	601532	GEN-23K	Human cysteine protease Mch2 isoform alpha (Mch2) mRNA, complete cds	1322	1244T>C	3
U20536	U20536	601532	GEN-23K	Human cysteine protease Mch2 isoform alpha (Mch2) mRNA, complete cds	1363	1285T>C	3
U24231	U24231	None	GEN-289	Human Fas-associating death domain-containing protein mRNA, complete cds	1312	1183G>A	3
U25029	U25029	138040	GEN-82	Glucocorticoid receptor alpha	335	335C>T	3
U25029	U25029	138040	GEN-82	Glucocorticoid receptor alpha	386	386T>C	3
U25029	U25029	138040	GEN-82	Glucocorticoid receptor alpha	1069	1069C>T	3
CDKN2A	U26727	600160	GEN-2BC	Human p16INK4/MTS1 mRNA, complete cds	311	284C>A	T95N
CDKN2A	U26727	600160	GEN-2BC	Human p16INK4/MTS1 mRNA, complete cds	570	543G>C	3
CDKN2A	U26727	600160	GEN-2BC	Human p16INK4/MTS1 mRNA, complete cds	643	616C>T	3
U27467	U27467	601056	GEN-2BX	Human Bcl-2 related (Bfl-1) mRNA, complete cds	476	442T>C	F148L
U27467	U27467	601056	GEN-2BX	Human Bcl-2 related (Bfl-1) mRNA, complete cds	481	447A>G	S
U27467	U27467	601056	GEN-2BX	Human Bcl-2 related (Bfl-1) mRNA, complete cds	542	508C>G	L170V
U27467	U27467	601056	GEN-2BX	Human Bcl-2 related (Bfl-1) mRNA, complete cds	578	544C>T	3
U27467	U27467	601056	GEN-2BX	Human Bcl-2 related (Bfl-1) mRNA, complete cds	614	580T>C	3

U27467	U27467	601056	GEN-2BX	Human Bcl-2 related (Bfl-1) mRNA, complete cds	616	582G>A	3
CSNK1D	U29171	600864	GEN-2E2	Human casein kinase I delta mRNA, complete cds	1612	1435C>A	3
U31628	U31628	601070	GEN-4J	Interleukin 15 receptor alpha chain	1250	1168G>T	3
U32324	U32324	600939	GEN-4K	interleukin 11 receptor alpha chain	1266	1205C>A	P402Q
U32324	U32324	600939	GEN-4K	interleukin 11 receptor alpha chain	1513	1452C>T	3
U33286	U33286	601342	GEN-IM	Chromosome segregation gene homolog CAS	54	(-70)A>G	5
U33286	U33286	601342	GEN-IM	Chromosome segregation gene homolog CAS	821	698G>A	G233D
U33286	U33286	601342	GEN-IM	Chromosome segregation gene homolog CAS	3127	3004T>C	3
FGF8	U36223	600483	GEN-2MX	Human fibroblast growth factor 8 (FGF-8) mRNA, complete cds	300	291T>C	S
FGF8	U36223	600483	GEN-2MX	Human fibroblast growth factor 8 (FGF-8) mRNA, complete cds	645	636G>C	S
FGF8	U36223	600483	GEN-2MX	Human fibroblast growth factor 8 (FGF-8) mRNA, complete cds	648	639A>G	S
U37448	U37448	601761	GEN-2OC	Human Mch3 isoform alpha (Mch3) mRNA, complete cds	736	693G>A	S
U37448	U37448	601761	GEN-2OC	Human Mch3 isoform alpha (Mch3) mRNA, complete cds	1285	1242T>C	3
U37448	U37448	601761	GEN-2OC	Human Mch3 isoform alpha (Mch3) mRNA, complete cds	1294	1251T>C	3
U37448	U37448	601761	GEN-2OC	Human Mch3 isoform alpha (Mch3) mRNA, complete cds	1580	1537A>T	3
U37448	U37448	601761	GEN-2OC	Human Mch3 isoform alpha (Mch3) mRNA, complete cds	1621	1578G>T	3
U37448	U37448	601761	GEN-2OC	Human Mch3 isoform alpha (Mch3) mRNA, complete cds	1715	1672G>A	3

U37448	U37448	601761	2OC	alpha (Mch3) mRNA, complete cds	1764	1721G>A	3
U37518	U37518	None	GEN- 2OC	Human Mch3 isoform alpha (Mch3) mRNA, complete cds	912	825C>T	S
U37518	U37518	None	GEN- 2OG	Human TNF-related apoptosis inducing ligand TRAIL mRNA, complete cds	1140	1053A>G	3
U37518	U37518	None	GEN- 2OG	Human TNF-related apoptosis inducing ligand TRAIL mRNA, complete cds	1289	1202C>A	3
U37518	U37518	None	GEN- 2OG	Human TNF-related apoptosis inducing ligand TRAIL mRNA, complete cds	1525	1438G>A	3
U37518	U37518	None	GEN- 2OG	Human TNF-related apoptosis inducing ligand TRAIL mRNA, complete cds	1588	1501G>A	3
U37518	U37518	None	GEN- 2OG	Human TNF-related apoptosis inducing ligand TRAIL mRNA, complete cds	1595	1508C>T	3
U39656	U39656	601254	GEN- 2Q8	Human MAP kinase kinase 6 (MKK6) mRNA, complete cds	431	91A>C	S
U39656	U39656	601254	GEN- 2Q8	Human MAP kinase kinase 6 (MKK6) mRNA, complete cds	713	373G>A	V125M
U43030	U43030	600435	GEN-LFI	Human cardiotrophin-1 (CTF1) mRNA, complete cds	1404	1372C>T	3
U43142	U43142	601528	GEN- 2UM	Human vascular endothelial growth factor related protein VRP cds	1499	1128C>T	S

U45878	U45878	601721	GEN- 2WJ	mRNA, complete cds Human inhibitor of apoptosis protein 1 mRNA, complete cds	2281	1833G>A	3
U45878	U45878	601721	GEN- 2WJ	Human inhibitor of apoptosis protein 1 mRNA, complete cds	2820	2372C>G	3
U45879	U45879	601712	GEN- 2WI	Human inhibitor of apoptosis protein 2 mRNA, complete cds	748	511T>G	S171A
U45879	U45879	601712	GEN- 2WI	Human inhibitor of apoptosis protein 2 mRNA, complete cds	835	598T>G	S200A
U47634	U47634	None	GEN- 2XR	Human beta-tubulin class III isotype (beta-3) mRNA, complete cds	1005	1005C>T	S
U47634	U47634	None	GEN- 2XR	Human beta-tubulin class III isotype (beta-3) mRNA, complete cds	1035	1035C>T	S
U47634	U47634	None	GEN- 2XR	Human beta-tubulin class III isotype (beta-3) mRNA, complete cds	1431	1431T>C	3
U47634	U47634	None	GEN- 2XR	Human beta-tubulin class III isotype (beta-3) mRNA, complete cds	1502	1502G>A	3
U54831	U54831	126431	GEN-8W	Topoisomerase II beta	127	127A>G	T43A
U54831	U54831	126431	GEN-8W	Topoisomerase II beta	1002	1002T>C	S
U55206	U55206	None	GEN- 35Z	Homo sapiens human gamma-glutamyl hydrolase (hGH) mRNA, complete cds	75	16T>C	C6R
U55206	U55206	None	GEN- 35Z	Homo sapiens human gamma-glutamyl hydrolase (hGH) mRNA, complete cds	150	91G>A	A31T
U55206	U55206	None	GEN- 35Z	Homo sapiens human gamma-glutamyl hydrolase (hGH) mRNA, complete cds	511	452C>T	T151I
U55206	U55206	None	GEN- 35Z	Homo sapiens human gamma-glutamyl hydrolase (hGH) mRNA, complete cds	1161	1102A>G	3

SD-144146.1

U56390	U56390	602234	GEN-36X	(hGH) mRNA, complete cds Human cysteine protease ICE-LAP6 mRNA, complete cds	411	408C>T	S
U60519	U60519	601762	GEN-3AZ	Human apoptotic cysteine protease Mch4 (Mch4) mRNA, complete cds	304	157G>A	E53K
U60519	U60519	601762	GEN-3AZ	Human apoptotic cysteine protease Mch4 (Mch4) mRNA, complete cds	324	177A>G	S
U70136	U70136	600044	GEN-4R	Thrombopoietin	4138	4105G>T	A1369S
U70136	U70136	600044	GEN-4R	Thrombopoietin	4141	4108T>A	F1370I
U70321	U70321	None	GEN-3K9	Human herpesvirus entry mediator mRNA, complete cds	343	50G>A	R17K
U70321	U70321	None	GEN-3K9	Human herpesvirus entry mediator mRNA, complete cds	1014	721G>A	V241I
U70321	U70321	None	GEN-3K9	Human herpesvirus entry mediator mRNA, complete cds	1218	925A>G	3
U70321	U70321	None	GEN-3K9	Human herpesvirus entry mediator mRNA, complete cds	1249	956C>T	3
U70321	U70321	None	GEN-3K9	Human herpesvirus entry mediator mRNA, complete cds	1453	1160G>A	3
U77088	U77088	188250	GEN-K4	Thymidine kinase 2	1480	1472T>C	3
U79269	U79269	123829	GEN-K7	Cyclin-Dependent Protein Kinase	1281	972A>T	3
U81375	U81375	602193	GEN-3VO	Human placental equilibrative nucleoside transporter 1 (hENT1) mRNA, complete cds	1989	1811G>A	3
U81375	U81375	602193	GEN-3VO	Human placental equilibrative nucleoside transporter 1 (hENT1) mRNA, complete cds	1996	1818C>T	3
U81375	U81375	602193	GEN-3VO	Human placental equilibrative nucleoside transporter 1 (hENT1) mRNA, complete cds	2045	1867T>C	3

IFNB1	V00546	147640	GEN-TV	transporter 1 (hENT1) mRNA, complete cds	474	410T>G	L137R
V00548	V00548	147562	GEN-P2	Messenger RNA for human fibroblast interferon	119	119G>A	R40K
V00594	V00594	156360	GEN-P6	Human messenger RNA for leukocyte (alpha-2) interferon	320	263G>C	3
EGFR	X00663	131550	GEN-U4	Human mRNA for metallothionein from cadmium-treated cells	1136	1136G>A	R379K
EGFR	X00663	131550	GEN-U4	Human mRNA fragment for epidermal growth factor (EGF) receptor	1935	1935A>G	S
EGFR	X00663	131550	GEN-U4	Human mRNA fragment for epidermal growth factor (EGF) receptor	2283	2283C>T	S
X00734	X00734	None	GEN-MST	Human beta-tubulin gene (5-beta) with ten Alu family members	1059	1059G>T	S
X00737	X00737	164050	GEN-P8	Human mRNA for purine nucleoside phosphorylase (PNP; EC 2.4.2.1)	59	(-51)T>G	5
X00737	X00737	164050	GEN-P8	Human mRNA for purine nucleoside phosphorylase (PNP; EC 2.4.2.1)	169	60T>C	S
X00737	X00737	164050	GEN-P8	Human mRNA for purine nucleoside phosphorylase (PNP; EC 2.4.2.1)	260	151A>G	S51G
X00737	X00737	164050	GEN-P8	Human mRNA for purine nucleoside phosphorylase (PNP; EC 2.4.2.1)	280	171T>C	S
X00737	X00737	164050	GEN-P8	Human mRNA for purine nucleoside phosphorylase (PNP; EC 2.4.2.1)	1254	1145G>A	3
X01060	X01060	190010	GEN-6C	Transferrin receptor (p90, CD71)	687	424A>G	S142G
X01060	X01060	190010	GEN-6C	Transferrin receptor (p90, CD71)	2823	2560delT	F

X01060	X01060	190010	GEN-6C	Transferrin receptor (p90, CD71)	3766	3503T>G	3
X01060	X01060	190010	GEN-6C	Transferrin receptor (p90, CD71)	4122	3859A>C	3
X01060	X01060	190010	GEN-6C	Transferrin receptor (p90, CD71)	4147	3884G>A	3
X01060	X01060	190010	GEN-6C	Transferrin receptor (p90, CD71)	4247	3984T>C	3
X01060	X01060	190010	GEN-6C	Transferrin receptor (p90, CD71)	4309	4046T>A	3
X01060	X01060	190010	GEN-6C	Transferrin receptor (p90, CD71)	4381	4118A>G	3
X01060	X01060	190010	GEN-6C	Transferrin receptor (p90, CD71)	4547	4284G>A	3
X01060	X01060	190010	GEN-6C	Transferrin receptor (p90, CD71)	4619	4356T>G	3
X01060	X01060	190010	GEN-6C	Transferrin receptor (p90, CD71)	4726	4463A>T	3
X01060	X01060	190010	GEN-6C	Transferrin receptor (p90, CD71)	4766	4503C>T	3
X01394	X01394	191160	GEN-4Y	Tumor necrosis factor	125	(-28)C>T	5
X01586	X01586	147680	GEN-PC	Interleukin 2	332	225T>G	H75Q
X01586	X01586	147680	GEN-PC	Interleukin 2	563	456G>A	S
X02308	X02308	188350	GEN-KL	Thymidylate synthetase	1066	961T>C	3
X02308	X02308	188350	GEN-KL	Thymidylate synthetase	1066	961T>C	3
X02308	X02308	188350	GEN-KL	Thymidylate synthetase	1136	1031A>G	3
X02308	X02308	188350	GEN-KL	Thymidylate synthetase	1136	1031A>G	3
X02308	X02308	188350	GEN-KL	Thymidylate synthetase	1497	1392T>A	3
X02469	X02469	191170	GEN-PF	Human mRNA for p53 cellular tumor antigen	350	215C>G	P72R
X02469	X02469	191170	GEN-PF	Human mRNA for p53 cellular tumor antigen	953	818G>A	R273H
NRAS	X02751	164790	GEN-XG	Human N-ras mRNA and flanking regions	221	(-506)A>G	5
NRAS	X02751	164790	GEN-XG	Human N-ras mRNA and flanking regions	390	(-337)C>A	5
X02812	X02812	190180	GEN-XR	Human mRNA for transforming growth factor-beta (TGF-beta)	870	29C>T	P10L
X02812	X02812	190180	GEN-XR	Human mRNA for transforming growth factor-beta (TGF-beta)	979	138C>G	I46M

X02812	X02812	190180	GEN-XR	transforming growth factor-beta (TGF-beta) Human mRNA for transforming growth factor-beta (TGF-beta)	1632	791C>T	T264I
X02812	X02812	190180	GEN-XR	transforming growth factor-beta (TGF-beta) Human mRNA for transforming growth factor-beta (TGF-beta)	1807	966C>T	S
X02812	X02812	190180	GEN-XR	transforming growth factor-beta (TGF-beta) Human mRNA for transforming growth factor-beta (TGF-beta)	1930	1089G>A	S
X02812	X02812	190180	GEN-XR	transforming growth factor-beta (TGF-beta) Human mRNA for transforming growth factor-beta (TGF-beta)	1942	1101C>T	S
X02812	X02812	190180	GEN-XR	transforming growth factor-beta (TGF-beta) Human mRNA for transforming growth factor-beta (TGF-beta)	2013	1172G>A	S391N
X03635	X03635	133430	GEN-50	estrogen receptors	390	30T>C	S
X03635	X03635	133430	GEN-50	estrogen receptors	390	30T>C	S
X03635	X03635	133430	GEN-50	estrogen receptors	424	64G>C	E22Q
X03635	X03635	133430	GEN-50	estrogen receptors	617	257C>T	A86V
X03635	X03635	133430	GEN-50	estrogen receptors	621	261G>C	S
X03635	X03635	133430	GEN-50	estrogen receptors	829	469C>T	F
X03635	X03635	133430	GEN-50	estrogen receptors	1335	975C>G	S
X03635	X03635	133430	GEN-50	estrogen receptors	1335	975C>G	S
X03635	X03635	133430	GEN-50	estrogen receptors	1451	1091T>A	V364E
X03635	X03635	133430	GEN-50	estrogen receptors	1674	1314G>A	M438I
X03635	X03635	133430	GEN-50	estrogen receptors	2142	1782A>G	S
X03635	X03635	133430	GEN-50	estrogen receptors	2354	1994A>G	3
X03635	X03635	133430	GEN-50	estrogen receptors	2550	2190A>C	3
X03635	X03635	133430	GEN-50	estrogen receptors	2733	2373C>G	3
X03635	X03635	133430	GEN-50	estrogen receptors	3181	2821T>C	3
X03635	X03635	133430	GEN-50	estrogen receptors	3338	2978C>T	3
X03635	X03635	133430	GEN-50	estrogen receptors	3652	3292-3294CCT>CC	3
X03635	X03635	133430	GEN-50	estrogen receptors	3652	3292-T	3
X03635	X03635	133430	GEN-50	estrogen receptors	3896	3294delCCT	3
				estrogen receptors		3536C>A	

X03635	X03635	133430	GEN-50	estrogen receptors	4378	4018T>C	3
X03635	X03635	133430	GEN-50	estrogen receptors	6287	5927T>C	3
X03663	X03663	164770	GEN-51	Colony stimulating factor 1 receptor	3732	3432T>C	3
X03663	X03663	164770	GEN-51	Colony stimulating factor 1 receptor	3951	3651C>A	3
X04571	X04571	131530	GEN-KY0	Human mRNA for kidney epidermal growth factor (EGF) precursor	4507	4071G>A	3
X04707	X04707	190160	GEN-CCA	Human c-erb-A mRNA for thyroid hormone receptor	1295	995T>C	I332T
ARAF1	X04790	311010	GEN-15C	Human mRNA for A-raf-1 oncogene	1659	1465C>T	F
KIT	X06182	164920	GEN-198	Human c-kit proto-oncogene mRNA	4656	4635G>T	3
ITGA5	X06256	135620	GEN-19B	Human mRNA for fibronectin receptor alpha subunit	2562	2539C>A	L847I
X06318	X06318	176970	GEN-KY	Protein kinase C, beta 1	83	(-54)G>C	5
X06318	X06318	176970	GEN-KY	Protein kinase C, beta 1	940	804G>A	S
X06318	X06318	176970	GEN-KY	Protein kinase C, beta 1	1327	1191T>C	S
X06318	X06318	176970	GEN-KY	Protein kinase C, beta 1	1906	1770C>T	S
RAF1	X06409	164760	GEN-19K	Human mRNA fragment for activated c-raf-1 (exons 8-17)	486	487T>C	3
RAF1	X06409	164760	GEN-19K	Human mRNA fragment for activated c-raf-1 (exons 8-17)	1947	1948C>T	3
RAF1	X06409	164760	GEN-19K	Human mRNA fragment for activated c-raf-1 (exons 8-17)	1992	1993C>A	3
GSTP1	X06547	134660	GEN-19N	Human mRNA for class Pi glutathione S-transferase (GST-Pi; E.C.2.5.1.18)	319	313A>G	I105V
GSTP1	X06547	134660	GEN-19N	Human mRNA for class Pi glutathione S-transferase (GST-Pi; E.C.2.5.1.18)	347	341C>T	A114V
GSTP1	X06547	134660	GEN-19N	Human mRNA for class Pi glutathione S-transferase (GST-Pi; E.C.2.5.1.18)	561	555C>T	S

ITGB1	X07979	135630	GEN-4E5	Human mRNA for fibronectin receptor beta subunit	1189	1086A>C	S
ITGB1	X07979	135630	GEN-4E5	Human mRNA for fibronectin receptor beta subunit	1279	1176A>C	S
ITGB1	X07979	135630	GEN-4E5	Human mRNA for fibronectin receptor beta subunit	2713	2610T>C	3
ITGB1	X07979	135630	GEN-4E5	Human mRNA for fibronectin receptor beta subunit	2878	2775T>A	3
ITGB1	X07979	135630	GEN-4E5	Human mRNA for fibronectin receptor beta subunit	3339	3236A>G	3
ITGB1	X07979	135630	GEN-4E5	Human mRNA for fibronectin receptor beta subunit	3531	3428G>A	3
ANX5	X12454	131230	GEN-1M2	Human mRNA for vascular anticoagulant	128	(-1)C>T	5
ANX5	X12454	131230	GEN-1M2	Human mRNA for vascular anticoagulant	1413	1285T>G	3
ANX5	X12454	131230	GEN-1M2	Human mRNA for vascular anticoagulant	1431	1303C>T	3
ANX5	X12454	131230	GEN-1M2	Human mRNA for vascular anticoagulant	1518	1390G>A	3
X12556	X12556	311030	GEN-1M8	Human mRNA for dbi proto-oncogene	2670	2496T>G	F832L
X13589	X13589	107910	GEN-56	Cytochrome P450, subfamily XIX (aromatization of androgens)	364	240A>G	S
X13589	X13589	107910	GEN-56	Cytochrome P450, subfamily XIX (aromatization of androgens)	914	790C>T	R264C
X13589	X13589	107910	GEN-56	Cytochrome P450, subfamily XIX (aromatization of androgens)	914	790C>T	R264C
X13589	X13589	107910	GEN-56	Cytochrome P450, subfamily XIX (aromatization of androgens)	1655	1531C>T	3

X13589	X13589	107910	GEN-56	subfamily XIX (aromatization of androgens) Cytochrome P450, subfamily XIX	1796	1672G>T	3
LIF	X13967	159540	GEN-1PZ	(aromatization of androgens) Human mRNA for leukaemia inhibitory factor (LIF/HILDA)	3710	3666T>G	3
CLU	X14723	185430	GEN-1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	131	84C>T	S
CLU	X14723	185430	GEN-1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	429	382G>T	V128F
CLU	X14723	185430	GEN-1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	836	789C>T	S
CLU	X14723	185430	GEN-1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	1234	1187C>T	S396L
CLU	X14723	185430	GEN-1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	1372	1325A>T	Y442F
CLU	X14723	185430	GEN-1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	1482	1435C>T	3
CLU	X14723	185430	GEN-1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	1548	1501C>T	3
CLU	X14723	185430	GEN-1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	1645	1598A>T	3

CSNK2B	X16312	115441	GEN-1XW	and beta-1 chain Human mRNA for phosvitin/casein kinase II	271	138T>C	S
CSNK2B	X16312	115441	GEN-1XW	beta subunit Human mRNA for phosvitin/casein kinase II	812	679A>T	3
CSNK2B	X16312	115441	GEN-1XW	beta subunit Human mRNA for phosvitin/casein kinase II	885	752T>C	3
X17033	X17033	192974	GEN-LG	beta subunit Integrin, alpha 2 (CD49B, alpha 2 subunit of VLA-2	4193	4145T>G	3
X17033	X17033	192974	GEN-LG	receptor) Integrin, alpha 2 (CD49B, alpha 2 subunit of VLA-2	4849	4801A>G	3
X17033	X17033	192974	GEN-LG	receptor) Integrin, alpha 2 (CD49B, alpha 2 subunit of VLA-2	4897	4849A>G	3
FGFR1	X51803	136350	GEN-32G	receptor) Human mRNA for fibroblast growth factor	276	159T>G	S
X51841	X51841	147557	GEN-21	(FGF) receptor Leukocyte integrin beta-4	4425	4299G>A	S
X51841	X51841	147557	GEN-21	Leukocyte integrin beta-4	4437	4311G>C	S
X51841	X51841	147557	GEN-21	Leukocyte integrin beta-4	4528	4402G>A	A1468T
X51841	X51841	147557	GEN-21	Leukocyte integrin beta-4	4821	4695C>T	S
X51841	X51841	147557	GEN-21	Leukocyte integrin beta-4	5157	5031C>T	S
X51841	X51841	147557	GEN-21	Leukocyte integrin beta-4	5184	5058G>A	S
X51841	X51841	147557	GEN-21	Leukocyte integrin beta-4	5252	5126C>T	P1709L
X51841	X51841	147557	GEN-21	Leukocyte integrin beta-4	5410	5284T>C	3
SPI1	X52056	165170	GEN-33A	Human mRNA for spi-1 proto-oncogene	1328	1117C>T	3
X52425	X52425	147781	GEN-59	Interleukin 4 receptor	3044	2869G>A	3
X52425	X52425	147781	GEN-59	Interleukin 4 receptor	3289	3114A>G	3
X52425	X52425	147781	GEN-59	Interleukin 4 receptor	3391	3216C>T	3
X52479	X52479	176960	GEN-LM	Protein kinase C, alpha	908	881A>C	D294A
FGFR2	X52832	176943	GEN-341	Human bek mRNA for fibroblast growth factor receptor-BEK	338	159A>G	S

SD-144146.1

FGFR2	X52832	176943	GEN-341	Human bek mRNA for fibroblast growth factor receptor-BEK	2903	2724A>T	3
X54199	X54199	138440	GEN-LS	Phosphoribosylglycinamide formyltransferase, phosphoribosylglycinamide synthetase, phosphoribosylaminoimidazole synthetase	168	90G>A	S
X54315	X54315	114020	GEN-351	Human mRNA for N-cadherin	2549	2448T>C	S
X55005	X55005	190120	GEN-35S	Human c-erbA-1 mRNA for thyroid hormone receptor alpha	493	27A>G	S
X55005	X55005	190120	GEN-35S	Human c-erbA-1 mRNA for thyroid hormone receptor alpha	1523	1057G>A	V353I
X55740	X55740	129190	GEN-36H	Human placental cDNA coding for 5nucleotidase (EC 3.1.3.5)	3373	3324T>G	3
X57110	X57110	165360	GEN-MKX	Cas-Br-M (murine) ecotropic retroviral transforming sequence	2695	2547T>A	S
FGFR4	X57205	134935	GEN-37M	Human FGFR-4 mRNA for fibroblast growth factor receptor (FGFR-4)	83	28G>A	V10I
FGFR4	X57205	134935	GEN-37M	Human FGFR-4 mRNA for fibroblast growth factor receptor (FGFR-4)	217	162T>G	S
GPX3	X58295	138321	GEN-38S	Human GPx-3 mRNA for plasma glutathione peroxidase	821	773C>T	3
GPX3	X58295	138321	GEN-38S	Human GPx-3 mRNA for plasma glutathione peroxidase	979	931G>A	3
GPX3	X58295	138321	GEN-38S	Human GPx-3 mRNA for plasma glutathione peroxidase	1187	1139T>G	3
GPX3	X58295	138321	GEN-38S	Human GPx-3 mRNA for plasma glutathione peroxidase	1354	1306C>T	3

GPX3	X58295	138321	GEN-38S	Human GPx-3 mRNA for plasma glutathione peroxidase	1443	1395C>T	3
GPX3	X58295	138321	GEN-38S	Human GPx-3 mRNA for plasma glutathione peroxidase	1516	1468C>A	3
GPX3	X58295	138321	GEN-38S	Human GPx-3 mRNA for plasma glutathione peroxidase	1581	1533C>T	3
X58377	X58377	147681	GEN-38V	Interleukin 11	807	744A>G	3
X58377	X58377	147681	GEN-38V	Interleukin 11	927	864T>G	3
X58377	X58377	147681	GEN-38V	Interleukin 11	1964	1901T>C	3
ITGA6	X59512	147556	GEN-39W	H.sapiens mRNA for integrin alpha6 subunit	186	186C>G	S
ITGA6	X59512	147556	GEN-39W	H.sapiens mRNA for integrin alpha6 subunit	188	188G>C	G63A
X59543	X59543	180410	GEN-M2	Ribonucleoside diphosphate reductase	1037	850C>A	S
X59543	X59543	180410	GEN-M2	Ribonucleoside diphosphate reductase	2410	2223G>A	S
X59543	X59543	180410	GEN-M2	Ribonucleoside diphosphate reductase	2410	2223G>A	S
X59543	X59543	180410	GEN-M2	Ribonucleoside diphosphate reductase	2419	2232A>G	S
X59543	X59543	180410	GEN-M2	Ribonucleoside diphosphate reductase	2717	2530T>A	3
X59543	X59543	180410	GEN-M2	Ribonucleoside diphosphate reductase	2724	2537^2538ins T	F
X59543	X59543	180410	GEN-M2	Ribonucleoside diphosphate reductase	2882	2695A>C	3
X59618	X59618	180390	GEN-M3	Ribonucleotide reductase M2 polypeptide	189	(-6)T>G	5
X59618	X59618	180390	GEN-M3	Ribonucleotide reductase M2 polypeptide	524	330C>G	S
X59618	X59618	180390	GEN-M3	Ribonucleotide reductase M2 polypeptide	1636	1442C>T	3
X59618	X59618	180390	GEN-M3	Ribonucleotide reductase M2 polypeptide	2259	2065T>C	3

NFKB2	X61498	164012	GEN-3BW	H.sapiens mRNA for NF-kB subunit	2457	2294C>T	P765L
KDR	X61656	191306	GEN-3BZ	H.sapiens mRNA for growth factor receptor tyrosine kinase	2308	2308A>G	T770A
KDR	X61656	191306	GEN-3BZ	H.sapiens mRNA for growth factor receptor tyrosine kinase	2353	2353G>C	G785R
KDR	X61656	191306	GEN-3BZ	H.sapiens mRNA for growth factor receptor tyrosine kinase	2499	2499C>G	N833K
KDR	X61656	191306	GEN-3BZ	H.sapiens mRNA for growth factor receptor tyrosine kinase	2537	2537A>T	E846V
KDR	X61656	191306	GEN-3BZ	H.sapiens mRNA for growth factor receptor tyrosine kinase	4123	4123G>C	3
DNMT	X63692	126375	GEN-3E4	H.sapiens mRNA for DNA methyltransferase (cytosin-5)-	4507	4270C>T	R1424C
DNMT	X63692	126375	GEN-3E4	H.sapiens mRNA for DNA methyltransferase (cytosin-5)-	4692	4455C>T	S
DNMT	X63692	126375	GEN-3E4	H.sapiens mRNA for DNA methyltransferase (cytosin-5)-	4922	4685C>A	T1562N
DNMT	X63692	126375	GEN-3E4	H.sapiens mRNA for DNA methyltransferase (cytosin-5)-	5235	4998C>T	3
X64177	X64177	156351	GEN-3EQ	H.sapiens mRNA for metallothionein	63	40G>A	A14T
X64177	X64177	156351	GEN-3EQ	H.sapiens mRNA for metallothionein	90	67A>G	K23E
X64177	X64177	156351	GEN-3EQ	H.sapiens mRNA for metallothionein	125	102C>T	S
X64177	X64177	156351	GEN-3EQ	H.sapiens mRNA for metallothionein	131	108T>C	S
X64177	X64177	156351	GEN-3EQ	H.sapiens mRNA for metallothionein	168	145A>G	I49V
X64177	X64177	156351	GEN-3EQ	H.sapiens mRNA for metallothionein	182	159G>A	S

SD-144146.1

X65019	X65019	147678	GEN-6G	INTERLEUKIN 1 BETA CONVERTASE PRECURSOR	51	44G>A	R15H
X65019	X65019	147678	GEN-6G	INTERLEUKIN 1 BETA CONVERTASE PRECURSOR	116	109A>C	K37Q
X65019	X65019	147678	GEN-6G	INTERLEUKIN 1 BETA CONVERTASE PRECURSOR	261	254G>A	G85E
X66364	X66364	123831	GEN-3GM	H.sapiens mRNA PSSALRE for serine/threonine protein kinase	495	471T>G	C157W
NTRK1	X66397	191315	GEN-3GN	H.sapiens tpr mRNA	2632	2335G>A	V779I
X69141	X69141	184420	GEN-3J9	H.sapiens mRNA for squalene synthase	112	21T>C	S
X69141	X69141	184420	GEN-3J9	H.sapiens mRNA for squalene synthase	292	201C>T	S
X69141	X69141	184420	GEN-3J9	H.sapiens mRNA for squalene synthase	1436	1345T>C	3
X69141	X69141	184420	GEN-3J9	H.sapiens mRNA for squalene synthase	1579	1488T>C	3
X69141	X69141	184420	GEN-3J9	H.sapiens mRNA for squalene synthase	1621	1530C>T	3
X69141	X69141	184420	GEN-3J9	H.sapiens mRNA for squalene synthase	1719	1628A>C	3
X69141	X69141	184420	GEN-3J9	H.sapiens mRNA for squalene synthase	1904	1813G>C	3
GPX4	X71973	138322	GEN-3L1	H.sapiens GPX-4 mRNA for phospholipid hydroperoxide glutathione peroxidase	718	638T>C	3
GPX4	X71973	138322	GEN-3L1	H.sapiens GPX-4 mRNA for phospholipid hydroperoxide glutathione peroxidase	837	757C>A	3
GPX4	X71973	138322	GEN-3L1	H.sapiens GPX-4 mRNA for phospholipid hydroperoxide glutathione peroxidase	882	802A>C	3

X75958	X75958	600456	GEN-3OE	H.sapiens trkB mRNA for protein-tyrosine kinase	30	(-68)C>G	5
X75958	X75958	600456	GEN-3OE	H.sapiens trkB mRNA for protein-tyrosine kinase	2010	1913A>G	3
X75958	X75958	600456	GEN-3OE	H.sapiens trkB mRNA for protein-tyrosine kinase	2101	2004C>T	3
X75962	X75962	600315	GEN-MNA	H.sapiens mRNA for OX40 homologue	836	831C>T	S
X76061	X76061	180203	GEN-3OK	H.sapiens p130 mRNA for 130K protein	685	616G>A	V206M
X76061	X76061	180203	GEN-3OK	H.sapiens p130 mRNA for 130K protein	2659	2590T>C	S
X76061	X76061	180203	GEN-3OK	H.sapiens p130 mRNA for 130K protein	3585	3516G>C	3
X76104	X76104	600831	GEN-3OO	H.sapiens DAP-kinase mRNA	4376	4040A>G	N1347S
X76105	X76105	600954	GEN-3ON	H.sapiens DAP-1 mRNA	887	728C>T	3
X76105	X76105	600954	GEN-3ON	H.sapiens DAP-1 mRNA	1089	930A>G	3
X76105	X76105	600954	GEN-3ON	H.sapiens DAP-1 mRNA	1890	1731A>G	3
X77722	X77722	602376	GEN-29	Interferon (alpha,beta, omega) receptor 2 (splice variant)	253	28G>T	V10F
X77722	X77722	602376	GEN-29	Interferon (alpha,beta, omega) receptor 2 (splice variant)	1128	903A>G	S
X77794	X77794	601578	GEN-N8	Cyclin G1	1133	1013G>A	3
X79389	X79389	600436	GEN-3T7	H.sapiens GSTT1 mRNA	824	824T>C	3
X79483	X79483	602399	GEN-LPR	H.sapiens ERK6 mRNA for extracellular signal regulated kinase	1287	1254T>G	3
X80230	X80230	603251	GEN-3UM	H.sapiens mRNA (clone C-2k) mRNA for serine/threonine protein kinase	25	(-74)C>T	5
X80230	X80230	603251	GEN-3UM	H.sapiens mRNA (clone C-2k) mRNA for serine/threonine protein kinase	77	(-22)C>T	5

X80230	X80230	603251	GEN-3UM	H.sapiens mRNA (clone C-2k) mRNA for serine/threonine protein kinase	1516	1418G>A	3
X80230	X80230	603251	GEN-3UM	H.sapiens mRNA (clone C-2k) mRNA for serine/threonine protein kinase	1574	1476A>G	3
X83544	X83544	602074	GEN-3Y6	H.sapiens DAP-3 mRNA	41	(-33)G>T	5
X83544	X83544	602074	GEN-3Y6	H.sapiens DAP-3 mRNA	285	212C>T	S71F
X83544	X83544	602074	GEN-3Y6	H.sapiens DAP-3 mRNA	294	221A>G	D74G
X83544	X83544	602074	GEN-3Y6	H.sapiens DAP-3 mRNA	877	804T>C	S
X83544	X83544	602074	GEN-3Y6	H.sapiens DAP-3 mRNA	1106	1033G>A	V345I
X83861	X83861	176806	GEN-5H	Prostaglandin E receptor 3 (subtype EP3) {alternative products}	387	180C>G	S
X84213	X84213	600516	GEN-3ZC	H.sapiens BAK mRNA for BCI-2 homologue	32	(-161)C>T	5
X84213	X84213	600516	GEN-3ZC	H.sapiens BAK mRNA for BCI-2 homologue	317	125G>A	R42H
X84213	X84213	600516	GEN-3ZC	H.sapiens BAK mRNA for BCI-2 homologue	435	243C>T	S
X84213	X84213	600516	GEN-3ZC	H.sapiens BAK mRNA for BCI-2 homologue	616	424G>A	V142I
X84213	X84213	600516	GEN-3ZC	H.sapiens BAK mRNA for BCI-2 homologue	663	471C>T	S
X84213	X84213	600516	GEN-3ZC	H.sapiens BAK mRNA for BCI-2 homologue	900	708T>C	3
X84213	X84213	600516	GEN-3ZC	H.sapiens BAK mRNA for BCI-2 homologue	974	782C>T	3
X86681	X86681	602110	GEN-41E	H.sapiens mRNA for nucleolar protein, HNP36	1725	1340G>A	3
X90858	X90858	191730	GEN-NQ	Uridine phosphorylase	309	(-44)C>T	5
X90858	X90858	191730	GEN-NQ	Uridine phosphorylase	824	472G>A	A158T
X92106	X92106	602403	GEN-	H.sapiens mRNA for	1405	1327A>G	I443V

X96395	X96395	601107	47S GEN-4AM	bleomycin hydrolase	848	811G>T	A271S
Y00285	Y00285	147280	GEN-6I	H.sapiens mRNA for canalicular multidrug resistance protein	4613	446G>A	S1489N
Y00285	Y00285	147280	GEN-6I	IGF-2 receptor	6371	6224C>T	T2075M
Y00285	Y00285	147280	GEN-6I	IGF-2 receptor	6813	666C>T	S
Y00285	Y00285	147280	GEN-6I	IGF-2 receptor	7150	7003G>A	V2335M
Y00285	Y00285	147280	GEN-6I	IGF-2 receptor	8685	8538C>A	3
GPX1	Y00433	138320	GEN-TJ	Human mRNA for glutathione peroxidase (EC 1.11.1.9.)	504	186G>A	S
GPX1	Y00433	138320	GEN-TJ	Human mRNA for glutathione peroxidase (EC 1.11.1.9.)	610	292C>G	R98G
GPX1	Y00433	138320	GEN-TJ	Human mRNA for glutathione peroxidase (EC 1.11.1.9.)	911	593C>T	P198L
GPX1	Y00433	138320	GEN-TJ	Human mRNA for glutathione peroxidase (EC 1.11.1.9.)	1048	730A>C	3
GPX1	Y00433	138320	GEN-TJ	Human mRNA for glutathione peroxidase (EC 1.11.1.9.)	1110	792A>C	3
Y00486	Y00486	102600	GEN-MGW	Human APRT gene for adenine phosphoribosyltransferase	503	432C>A	S
Y00486	Y00486	102600	GEN-MGW	Human APRT gene for adenine phosphoribosyltransferase	505	434G>C	R145P
Y00486	Y00486	102600	GEN-MGW	Human APRT gene for adenine phosphoribosyltransferase	792	721A>G	3
PAI2	Y00630	173390	GEN-U6	Human mRNA for Arg-Serpin (plasminogen activator-inhibitor 2, PAI-2)	430	358A>G	N120D
PAI2	Y00630	173390	GEN-U6	Human mRNA for Arg-Serpin (plasminogen activator-inhibitor 2, PAI-2)	1251	1179T>G	S
PAI2	Y00630	173390	GEN-U6	Human mRNA for Arg-Serpin (plasminogen activator-inhibitor 2, PAI-2)	1762	1690G>A	3

OAT	Y07511	258870	GEN-1E3	Serpin (plasminogen activator-inhibitor 2, PAI-2)	1174	1134C>T	S
OAT	Y07511	258870	GEN-1E3	Human mRNA for kidney ornithine aminotransferase (EC 2.6.1.13)	1545	1505C>T	3
Y08200	Y08200	601905	GEN-1FT	Human mRNA for kidney ornithine aminotransferase (EC 2.6.1.13)	1696	1422C>T	S
Y08201	Y08201	179080	GEN-9B	Homo sapiens mRNA for rab geranylgeranyl transferase, alpha-subunit	54	51T>A	S
Y10659	Y10659	300119	GEN-1J6	Geranylgeranyl transferase type II beta-subunit	1116	1073G>A	G358D
Z11695	Z11695	176948	GEN-1L1	H.sapiens IL-13Ra mRNA	1287	1153G>A	3
Z11696	Z11696	601795	GEN-1L0	H.sapiens 40 kDa protein kinase related to rat ERK2	449	449T>G	I150S
Z14138	Z14138	603259	GEN-1QS	H.sapiens 44kDa protein kinase related to rat ERK1	394	234T>C	S
				H.sapiens (Ewings sarcoma cell line) mRNA encoding open reading frame			
Z15108	Z15108	176982	GEN-1TE	H.sapiens mRNA for protein kinase C zeta	246	240T>C	S
Z15108	Z15108	176982	GEN-1TE	H.sapiens mRNA for protein kinase C zeta	1694	1688A>C	D563A
Z15108	Z15108	176982	GEN-1TE	H.sapiens mRNA for protein kinase C zeta	2033	2027G>A	3
Z15108	Z15108	176982	GEN-1TE	H.sapiens mRNA for protein kinase C zeta	2086	2080T>G	3
Z35491	Z35491	601497	GEN-2ME	H.sapiens mRNA for novel glucocorticoid receptor-associated protein	315	37G>A	E13K
Z35491	Z35491	601497	GEN-2ME	H.sapiens mRNA for novel glucocorticoid receptor-associated protein	333	55G>A	E19K
Z35491	Z35491	601497	GEN-2ME	H.sapiens mRNA for novel glucocorticoid receptor-associated protein	1297	1019A>C	3
CCNF	Z36714	600227	GEN-2NB	H.sapiens mRNA for cyclin F	4062	4019C>A	3

Z48810 Z48810 602664 GEN- 1280 1239A>C 3

H.sapiens mRNA for TX
protease precursor

Table 13.
Identified
Variances
In Genes
for
Pathways
Identified
in
Neurologi
cal and
Psychiatri
c
Diseases

AB00026	AB00026	602784	GEN- 16N	215 210T>C	S
3	3				
Human mRNA for prepro cortistatin like peptide, complete cds					
AB00063	AB00063	601646	GEN-169	1423 1409T>C	L470P
4	4				
Homo sapiens mRNA for protein phosphatase 2A delta (B) regulatory subunit, delta1 isoform, complete cds					
AB00063	AB00063	601646	GEN-169	2163 2149T>A	3
4	4				
Homo sapiens mRNA for protein phosphatase 2A delta (B) regulatory subunit, delta1 isoform, complete cds					
AB00234	AB00234	601581	GEN- 1CR	2562 2148G>C	S
1	1				
Human mRNA for KIAA0343 gene, complete cds					
AB00255	AB00255	601717	GEN- 1AA	1467 1443T>C	S
9	9				
hunc18b2, complete cds					
AB00255	AB00255	601717	GEN- 1AA	1600 1576G>A	V526I
9	9				
hunc18b2, complete cds					
AB00255	AB00255	601717	GEN- 1AA	1669 1645G>A	A549T
9	9				
hunc18b2, complete cds					
AB00591	AB00591	602758	GEN-VC	891 822C>T	S
0	0				
Homo sapiens mRNA for phosphatidylinositol 4-					

SD-144146.1

AB01071	AB01071	602601	GEN-1SQ	kinase, complete cds	1071 1010T>A	3
	0	0		Homo sapiens mRNA for lectin-like oxidized LDL receptor, complete cds		
AB01071	AB01071	602601	GEN-1SQ	Homo sapiens mRNA for lectin-like oxidized LDL receptor, complete cds	1073 1012T>C	3
	0	0				
AB01071	AB01071	602601	GEN-1SQ	Homo sapiens mRNA for lectin-like oxidized LDL receptor, complete cds	1073 1012T>C	3
	0	0				
AB01071	AB01071	602601	GEN-1SQ	Homo sapiens mRNA for lectin-like oxidized LDL receptor, complete cds	1801 1740A>G	3
	0	0				
AB01071	AB01071	602601	GEN-1SQ	Homo sapiens mRNA for lectin-like oxidized LDL receptor, complete cds	2199 2138G>A	3
	0	0				
AB01388	AB01388	603208	GEN-CBP	Inward rectifier potassium channel Kir 1.4	1469 1218A>G	3
AB01531	AB01531	None	GEN-L2T	Homo sapiens mRNA for gamma2-adaptin, complete cds	377 332A>G	D111G
	8	8				
AB01531	AB01531	None	GEN-L2T	Homo sapiens mRNA for gamma2-adaptin, complete cds	534 489G>A	S
	8	8				
AB01531	AB01531	None	GEN-L2T	Homo sapiens mRNA for gamma2-adaptin, complete cds	2444 2399C>A	3
	8	8				
AF000234	AF000234	600846	GEN-16J	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 4; P2RX4	365 365C>T	P122L
AF000234	AF000234	600846	GEN-16J	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 4; P2RX4	381 381G>A	S
AF000234	AF000234	600846	GEN-16J	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 4; P2RX4	624 624A>G	S
AF000234	AF000234	600846	GEN-16J	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 4; P2RX4	641 641C>T	P214L
AF000234	AF000234	600846	GEN-16J	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 4; P2RX4	1161 1161T>C	3

AF004562	AF004562	602926	GEN-UK	CHANNEL, 4; P2RX4 Homo sapiens hUNC18a alternatively-spliced mRNA, complete cds	1830 1710A>T	S
AF004562	AF004562	602926	GEN-UK	Homo sapiens hUNC18a alternatively-spliced mRNA, complete cds	3322 3202T>C	3
AF004562	AF004562	602926	GEN-UK	Homo sapiens hUNC18a alternatively-spliced mRNA, complete cds	3673 3553C>G	3
AF006823	AF006823	603220	GEN-WS	Homo sapiens TWIK- related acid-sensitive K+ channel (TASK) mRNA, complete cds	1160 1035G>A	S
AF007548	AF007548	None	GEN-12G	Homo sapiens golgi SNARE (GS27) mRNA, complete cds	200 200G>A	R67K
AF010126	AF010126	602998	GEN-1SR	Homo sapiens breast cancer-specific protein 1 (BCSG1) mRNA, complete cds	206 195C>G	S
AF010126	AF010126	602998	GEN-1SR	Homo sapiens breast cancer-specific protein 1 (BCSG1) mRNA, complete cds	340 329A>T	E110V
AF010126	AF010126	602998	GEN-1SR	Homo sapiens breast cancer-specific protein 1 (BCSG1) mRNA, complete cds	518 507C>T	3
AF016709	AF016709	602836	GEN-1NE	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 5; P2RX5	1023 987T>C	S
AF016709	AF016709	602836	GEN-1NE	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 5; P2RX5	1025 989T>C	F330S
AF016709	AF016709	602836	GEN-1NE	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 5; P2RX5	1090 1054G>C	E352Q
AF016709	AF016709	602836	GEN-1NE	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 5; P2RX5	1321 1285G>A	3

AF016709	AF016709	602836	GEN-1NE	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 5; P2RX5	1424 1388C>G	3
AF016709	AF016709	602836	GEN-1NE	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 5; P2RX5	1512 1476G>A	3
AF016709	AF016709	602836	GEN-1NE	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 5; P2RX5	1743 1707A>G	3
AF016709	AF016709	602836	GEN-1NE	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 5; P2RX5	1858 1822A>G	3
AF016903	AF016903	None	GEN-1M7	Homo sapiens agrin precursor mRNA, partial cds	516 516C>G	S
AF016903	AF016903	None	GEN-1M7	Homo sapiens agrin precursor mRNA, partial cds	518 518G>C	R173P
AF016903	AF016903	None	GEN-1M7	Homo sapiens agrin precursor mRNA, partial cds	3501 3501C>T	S
AF016903	AF016903	None	GEN-1M7	Homo sapiens agrin precursor mRNA, partial cds	6422 6422A>G	3
AF016903	AF016903	None	GEN-1M7	Homo sapiens agrin precursor mRNA, partial cds	6704 6704A>G	3
HRH1	AF026261	600167	GEN-26W	Histamine receptor H1	1068 1068A>G	S
AVPR1B	AF030512	600264	GEN-4FF	Homo sapiens small cell vasopressin subtype 1b receptor mRNA, complete cds	273 150G>A	S
AF030625	AF030625	600821	GEN-2	Vasopressin V1A receptor	314 291C>T	S
AF030625	AF030625	600821	GEN-2	Vasopressin V1A receptor	431 408T>C	S
AF030625	AF030625	600821	GEN-2	Vasopressin V1A receptor	506 483A>G	S
AF033382	AF033382	603787	GEN-2OT	potassium channel	476 476G>T	G159V
AF033382	AF033382	603787	GEN-2OT	potassium channel	1083 1083C>T	S
AF034795	AF034795	116935	GEN-	Homo sapiens cell matrix	1404 853G>A	3

SD-144146.1

AF034795	AF034795	116935	2GB	adhesion regulator variant (CMAR) mRNA, complete cds	1411 860C>T	3
AF034795	AF034795	116935	GEN-2GB	Homo sapiens cell matrix adhesion regulator variant (CMAR) mRNA, complete cds	1811 1260G>A	3
TUBB	AF035316	191130	GEN-2IH	Homo sapiens clone 23678 mRNA, partial cds	273 273G>A	F
TUBB	AF035316	191130	GEN-2IH	Homo sapiens clone 23678 mRNA, partial cds	295 295G>C	A99P
TUBB	AF035316	191130	GEN-2IH	Homo sapiens clone 23678 mRNA, partial cds	302 302C>T	T101I
TUBB	AF035316	191130	GEN-2IH	Homo sapiens clone 23678 mRNA, partial cds	1059 1059G>A	3
AF036892	AF036892	601937	GEN-7W	Nuclear receptor coactivator (ACTR)	842 659G>T	R220I
AF036892	AF036892	601937	GEN-7W	Nuclear receptor coactivator (ACTR)	1971 1788G>C	Q596H
AF036892	AF036892	601937	GEN-7W	Nuclear receptor coactivator (ACTR)	3048 2865A>G	S
AF036892	AF036892	601937	GEN-7W	Nuclear receptor coactivator (ACTR)	3909 3726A>G	S
AF036892	AF036892	601937	GEN-7W	Nuclear receptor coactivator (ACTR)	4483 4300T>C	3
AF036892	AF036892	601937	GEN-7W	Nuclear receptor coactivator (ACTR)	5644 5461A>G	3
AF036892	AF036892	601937	GEN-7W	Nuclear receptor coactivator (ACTR)	5675 5492T>A	3
AF036892	AF036892	601937	GEN-7W	Nuclear receptor coactivator (ACTR)	6051 5868T>G	3
AF036892	AF036892	601937	GEN-7W	Nuclear receptor coactivator (ACTR)	6664 6481G>A	3
AF038173	AF038173	601255	GEN-2QH	Homo sapiens clone 23723 axonal transporter of synaptic vesicles (ATSV) mRNA, partial cds	1368 1368T>C	3

AF038173	AF038173	601255	GEN- 2QH	Homo sapiens clone 23723 axonal transporter of synaptic vesicles (ATSV) mRNA, partial cds	1387 1387A>G	3
AF038173	AF038173	601255	GEN- 2QH	Homo sapiens clone 23723 axonal transporter of synaptic vesicles (ATSV) mRNA, partial cds	1501 1501G>C	3
AF039400	AF039400	603906	GEN- MQY	Homo sapiens calcium- dependent chloride channel-1 (hCLCA1) mRNA, complete cds	2787 2436T>C	S
AF043472	AF043472	603888	GEN- 2XX	Homo sapiens Shab- related delayed-rectifier K+ channel alpha subunit (KCNK3) mRNA, complete cds	1840 1709T>G	3
AF043473	AF043473	602905	GEN- 2XW	POTASSIUM CHANNEL PROTEIN KV2.1	1308 1308G>T	S
AF046873	AF046873	602705	GEN- LFF	Homo sapiens synapsin IIIa mRNA, complete cds	1364 1328G>A	R443H
AF047442	AF047442	None	GEN- LFO	Homo sapiens vesicle trafficking protein sec22b mRNA, complete cds	160 96G>A	S
AF048837	AF048837	602973	GEN- LGG	Homo sapiens cGMP- specific phosphodiesterase (PDE9A2) mRNA, complete cds	1551 1491T>C	S
AF052224	AF052224	None	GEN- MR1	Homo sapiens neuronal double zinc finger protein (ZNF231) mRNA, complete cds	15480 15365T>G	3
AF052224	AF052224	None	GEN- MR1	Homo sapiens neuronal double zinc finger protein (ZNF231) mRNA, complete cds	15560 15445C>T	3
AF052224	AF052224	None	GEN- MR1	Homo sapiens neuronal double zinc finger protein (ZNF231) mRNA, complete cds	15745 15630C>T	3
AF053233	AF053233	None	GEN-	Homo sapiens endobrevin cds	225 201A>G	S

AF058921	AF058921	None	38F GEN- LJY	mRNA, complete cds Homo sapiens cytosolic phospholipase A2-gamma mRNA, complete cds	1972 1663G>A	3
AF058921	AF058921	None	GEN- LJY	Homo sapiens cytosolic phospholipase A2-gamma mRNA, complete cds	1989 1680A>T	3
AF060538	AF060538	185880	GEN-LL4	Homo sapiens vesicle associated membrane protein-1B mRNA, alternatively spliced, complete cds	780 650C>T	3
AF064548	AF064548	603506	GEN- KV4	Homo sapiens low-density lipoprotein receptor-related protein 5 (LRP5) mRNA, complete cds	1695 1647C>T	S
AF064548	AF064548	603506	GEN- KV4	Homo sapiens low-density lipoprotein receptor-related protein 5 (LRP5) mRNA, complete cds	4037 3989C>T	A1330V
AF064548	AF064548	603506	GEN- KV4	Homo sapiens low-density lipoprotein receptor-related protein 5 (LRP5) mRNA, complete cds	4683 4635C>A	S
AF064548	AF064548	603506	GEN- KV4	Homo sapiens low-density lipoprotein receptor-related protein 5 (LRP5) mRNA, complete cds	4802 4754C>T	S1585L
AF077671	AF077671	600755	GEN- LMT	Homo sapiens synapsin IIa (SYN2) mRNA, complete cds	1246 1225T>C	S
AJ130763	AJ130763	254780	GEN- LDP	Homo sapiens mRNA for LAFPTase, isoform 1, partial	161 159G>A	S
AJ130763	AJ130763	254780	GEN- LDP	Homo sapiens mRNA for LAFPTase, isoform 1, partial	287 285T>A	S
D12614	D12614	153440	GEN-QD	Human mRNA for lymphotoxin (TNF-beta), complete cds	319 179C>A	T60N
D13388	D13388	602837	GEN-A7	DNAJ PROTEIN	207 90C>T	S

SD-144146.1

CYP11B2	D13752	124080	GEN-CCD	HOMOLOG 2 Human CYP11B2 gene for steroid 18-hydroxylase, complete cds	1600 1593G>A	3
D13811	D13811	238310	GEN-AA	Glycine cleavage system: Protein T	277 148G>T	V50L
D13811	D13811	238310	GEN-AA	Glycine cleavage system: Protein T	1073 944G>A	R315K
D13811	D13811	238310	GEN-AA	Glycine cleavage system: Protein T	1083 954G>A	S
D13811	D13811	238310	GEN-AA	Glycine cleavage system: Protein T	1773 1644C>T	3
D13811	D13811	238310	GEN-AA	Glycine cleavage system: Protein T	2037 1908C>T	3
D16469	D16469	300197	GEN-1Y2	Human mRNA for ORF, Xq terminal portion	2294 941A>G	3
D16469	D16469	300197	GEN-1Y2	Human mRNA for ORF, Xq terminal portion	2460 1107A>G	3
D16469	D16469	300197	GEN-1Y2	Human mRNA for ORF, Xq terminal portion	2660 1307C>A	3
D25235	D25235	104221	GEN-3	Adrenergic receptor alpha 1c	1035 599T>G	I200S
D25235	D25235	104221	GEN-3	Adrenergic receptor alpha 1c	1475 1039C>T	R347C
D25235	D25235	104221	GEN-3	Adrenergic receptor alpha 1c	1475 1039C>T	R347C
D25235	D25235	104221	GEN-3	Adrenergic receptor alpha 1c	2048 1612C>T	3
D25418	D25418	600022	GEN-78	Prostaglandin I2 (prostaglandin) receptor (IP)	726 635G>A	R212H
D25418	D25418	600022	GEN-78	Prostaglandin I2 (prostaglandin) receptor (IP)	1047 956C>G	S319W
D25418	D25418	600022	GEN-78	Prostaglandin I2 (prostaglandin) receptor (IP)	1075 984A>C	S
D28538	D28538	604102	GEN-2DC	Metabotropic glutamate receptor type 5	531 381A>G	S
D32051	D32051	138440	GEN-4	Glycinamide ribonucleotide transformylase	25 (-47)G>A	5
D32051	D32051	138440	GEN-4	Glycinamide ribonucleotide transformylase	1332 1261A>G	I421V
D32051	D32051	138440	GEN-4	Glycinamide ribonucleotide transformylase	1855 1784G>C	3

PTGIR	D38128	600022	GEN-4DH	transformylase Human IP gene for prostacyclin receptor, exon 3	203 204C>G	3
PTGIR	D38128	600022	GEN-4DH	Human IP gene for prostacyclin receptor, exon 3	231 232C>A	3
D38145	D38145	601699	GEN-4E3	Human mRNA for prostacyclin synthase, complete cds	1646 1619T>C	3
D45887	D45887	114182	GEN-BA	Calmodulin 1 (phosphorylase kinase, delta)	34 (-35)G>T	5
D49394	D49394	182139	GEN-5	Serotonin 5-HT receptors 5-HT3	1914 1695C>G	3
D50678	D50678	602600	GEN-30Y	Human mRNA for apolipoprotein E receptor 2, complete cds	3378 3276G>A	3
D50678	D50678	602600	GEN-30Y	Human mRNA for apolipoprotein E receptor 2, complete cds	3755 3653G>A	3
D50678	D50678	602600	GEN-30Y	Human mRNA for apolipoprotein E receptor 2, complete cds	3949 3847G>C	3
D50678	D50678	602600	GEN-30Y	Human mRNA for apolipoprotein E receptor 2, complete cds	4368 4266T>A	3
D50678	D50678	602600	GEN-30Y	Human mRNA for apolipoprotein E receptor 2, complete cds	4455 4353G>A	3
D87673	D87673	602438	GEN-444	Human mRNA for heat shock transcription factor 4, complete cds	274 270C>T	S
D87673	D87673	602438	GEN-444	Human mRNA for heat shock transcription factor 4, complete cds	1463 1459G>C	3
D87845	D87845	602344	GEN-44C	Human mRNA for platelet-activating factor acetylhydrolase 2, complete cds	2299 2096G>A	3
D87845	D87845	602344	GEN-	Human mRNA for platelet-	2332 2129A>G	3

D89052	D89052	603717	44C	activating factor acetylhydrolase 2, complete cds	56 (-27)G>T	5
D89052	D89052	603717	GEN-45C	Human mRNA for proton-ATPase-like protein, complete cds	719 637G>A	3
D89078	D89078	601531	GEN-7	P2Y7 purinoceptor	434 (-1284)A>T	5
D89078	D89078	601531	GEN-7	P2Y7 purinoceptor	889 (-829)G>C	5
D89078	D89078	601531	GEN-7	P2Y7 purinoceptor	1156 (-562)G>C	5
D89078	D89078	601531	GEN-7	P2Y7 purinoceptor	2644 927T>C	S
D89078	D89078	601531	GEN-7	P2Y7 purinoceptor	2920 1203A>G	3
LRP1	D90070	107770	GEN-466	Human ATL-derived PMA-responsive (APR) peptide mRNA	686 513T>G	3
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	1449 969C>T	S
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	1449 969C>T	S
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	1485 1005A>G	S
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	1485 1005A>G	S
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	1834 1354C>G	3
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	1834 1354C>G	3
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	2228 1748G>A	3
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	2376 1896G>A	3
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	2764 2284G>A	3
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	2764 2284G>A	3
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	2840 2360G>C	3
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	2935 2455G>A	3

EDNRA	D90348	131243	4DX GEN-4DX	Endothelin Receptor Type A	3294 2814A>G	3
J00123	J00123	131330	GEN-MK4	Human enkephalin gene	81 81C>T	S
FGA	J00127	134820	GEN-T3	Human fibrinogen alpha-chain mRNA, complete cds	560 530T>A	I177N
FGA	J00127	134820	GEN-T3	Human fibrinogen alpha-chain mRNA, complete cds	1138 1108G>T	A370S
J00129	J00129	134830	GEN-T4	Human fibrinogen beta-chain mRNA, partial cds	543 543C>T	S
J00129	J00129	134830	GEN-T4	Human fibrinogen beta-chain mRNA, partial cds	1101 1101C>T	S
J00129	J00129	134830	GEN-T4	Human fibrinogen beta-chain mRNA, partial cds	1409 1409G>A	R470K
J00137	J00137	306900	GEN-OX	COAGULATION FACTOR IX	581 580A>G	T194A
DHFR	J00140	126060	GEN-4E9	Human dihydrofolate reductase gene	721 679T>A	3
DHFR	J00140	126060	GEN-4E9	Human dihydrofolate reductase gene	721 679T>A	3
DHFR	J00140	126060	GEN-4E9	Human dihydrofolate reductase gene	829 787C>T	3
J02611	J02611	107740	GEN-6O	Human apolipoprotein D mRNA, complete cds	676 615T>G	3
J02611	J02611	107740	GEN-6O	Human apolipoprotein D mRNA, complete cds	683 622T>G	3
J02611	J02611	107740	GEN-6O	Human apolipoprotein D mRNA, complete cds	701 640C>G	3
J02611	J02611	107740	GEN-6O	Human apolipoprotein D mRNA, complete cds	745 684A>G	3
CBG	J02943	122500	GEN-Y2	Human corticosteroid binding globulin mRNA, complete cds	106 71A>T	D24V
CBG	J02943	122500	GEN-Y2	Human corticosteroid binding globulin mRNA, complete cds	971 936T>C	S
CBG	J02943	122500	GEN-Y2	Human corticosteroid binding globulin mRNA, complete cds	1229 1194G>A	S
J03143	J03143	107470	GEN-ZK	Human interferon-gamma	1098 1050T>G	S

J03242	J03242	147470	GEN-PJ	receptor mRNA, complete cds	932 380G>A	R127H
J03242	J03242	147470	GEN-PJ	Insulin-like growth factor 2	1063 511G>A	A171T
J03242	J03242	147470	GEN-PJ	Insulin-like growth factor 2	1190 638C>G	3
J03242	J03242	147470	GEN-PJ	Insulin-like growth factor 2	1201 649C>T	3
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	172 57C>T	S
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	559 444C>T	S
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	1704 1589C>A	3
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	1833 1718C>G	3
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	1959 1844A>C	3
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	3301 3186C>A	3
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	3991 3876A>G	3
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	4187 4072G>A	3
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	4187 4072G>A	3
CHGA	J03483	118910	GEN-11E	Human chromogranin A mRNA, complete cds	583 501T>G	N167K
CHGA	J03483	118910	GEN-11E	Human chromogranin A mRNA, complete cds	1405 1323A>G	S
CHGA	J03483	118910	GEN-11E	Human chromogranin A mRNA, complete cds	1543 1461C>T	3

J03490	J03490	246900	GEN-C5	Dihydrolipoamide dehydrogenase (E3 component of pyruvate dehydrogenase complex, 2-oxo-glutarate complex, branched chain keto acid dehydrogenase complex)	1569 1493A>C	N498T
J03490	J03490	246900	GEN-C5	Dihydrolipoamide dehydrogenase (E3 component of pyruvate dehydrogenase complex, 2-oxo-glutarate complex, branched chain keto acid dehydrogenase complex)	1624 1548T>A	3
J03490	J03490	246900	GEN-C5	Dihydrolipoamide dehydrogenase (E3 component of pyruvate dehydrogenase complex, 2-oxo-glutarate complex, branched chain keto acid dehydrogenase complex)	1813 1737A>G	3
J03490	J03490	246900	GEN-C5	Dihydrolipoamide dehydrogenase (E3 component of pyruvate dehydrogenase complex, 2-oxo-glutarate complex, branched chain keto acid dehydrogenase complex)	2096 2020T>C	3
J03778	J03778	157140	GEN-C7	MICROTUBULE- ASSOCIATED PROTEIN TAU	391 354G>A	S
J03853	J03853	104250	GEN-A	Adrenergic receptor alpha 2c	1202 1164C>T	S
J03853	J03853	104250	GEN-A	Adrenergic receptor alpha 2c	1237 1199T>G	I400S
J03853	J03853	104250	GEN-A	Adrenergic receptor alpha 2c	1372 1334C>G	P445R
J03853	J03853	104250	GEN-A	Adrenergic receptor alpha 2c	1379 1341C>T	S
J04031	J04031	172460	GEN-CB	Methenyltetrahydrofolate cyclohydrolase	454 401G>A	R134K

SD-144146.1

J04031	J04031	172460	GEN-CB	Methenyltetrahydrofolate cyclohydrolase	969 916C>G	Q306E
J04031	J04031	172460	GEN-CB	Methenyltetrahydrofolate cyclohydrolase	1614 1561T>C	S
J04031	J04031	172460	GEN-CB	Methenyltetrahydrofolate cyclohydrolase	2011 1958G>A	R653Q
J04031	J04031	172460	GEN-CB	Methenyltetrahydrofolate cyclohydrolase	2335 2282C>T	T761M
J04046	J04046	114183	GEN- 13N	Human calmodulin mRNA, complete cds	791 688C>T	3
J04046	J04046	114183	GEN- 13N	Human calmodulin mRNA, complete cds	881 778T>C	3
J04046	J04046	114183	GEN- 13N	Human calmodulin mRNA, complete cds	1927 1824T>C	3
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	803 781G>T	A261S
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	1042 1020C>T	S
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	1535 1513- 1515CCT>CC T	S
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	1535 1513- 1515delCCT 6-505del]	[P505V;50 6-505del] D592G
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	1797 1775A>G	S
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	2215 2193G>A	S
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	2350 2328A>G	S
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	2505 2483T>C	M828T
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	3409 3387T>C	S
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	3409 3387T>C	S
J05158	J05158	603104	GEN-173	Human carboxypeptidase N mRNA, 3 end	2314 2314C>T	3
J05158	J05158	603104	GEN-173	Human carboxypeptidase N mRNA, 3 end	2316 2316G>T	3
J05158	J05158	603104	GEN-173	Human carboxypeptidase N mRNA, 3 end	2332 2332G>T	3

J05158	J05158	603104	GEN-173	Human carboxypeptidase N mRNA, 3 end	2541 2541G>A	3
J05158	J05158	603104	GEN-173	Human carboxypeptidase N mRNA, 3 end	2651 2651C>T	3
J05176	J05176	107280	GEN-PT	Human alpha-1- antichymotrypsin mRNA, 3 end	240 240A>G	S
J05176	J05176	107280	GEN-PT	Human alpha-1- antichymotrypsin mRNA, 3 end	327 327C>T	S
J05176	J05176	107280	GEN-PT	Human alpha-1- antichymotrypsin mRNA, 3 end	554 554T>C	V185A
J05200	J05200	180901	GEN-17B	Human ryanodine receptor mRNA, complete cds	14981 14876G>T	G4959V
J05594	J05594	601688	GEN-E	Prostaglandin 15-OH dehydrogenase (PGDH)	173 156A>G	S
J05594	J05594	601688	GEN-E	Prostaglandin 15-OH dehydrogenase (PGDH)	913 896C>G	3
J05594	J05594	601688	GEN-E	Prostaglandin 15-OH dehydrogenase (PGDH)	950 933G>A	3
J05594	J05594	601688	GEN-E	Prostaglandin 15-OH dehydrogenase (PGDH)	1448 1431G>A	3
J05594	J05594	601688	GEN-E	Prostaglandin 15-OH dehydrogenase (PGDH)	1972 1955T>C	3
J05594	J05594	601688	GEN-E	Prostaglandin 15-OH dehydrogenase (PGDH)	1972 1955T>C	3
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	121 61G>A	E21K
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	151 91G>A	E31K
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	197 137T>C	L46P
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	204 144delG	F
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	238 178A>G	T60A

K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	365 305C>G	P102R
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	409 349G>A	A117T
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	448 388T>C	C130R
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	494 434G>A	G145D
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	515 455G>A	R152Q
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	520 460C>A	R154S
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	538 478C>T	R160C
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	547 487C>T	R163C
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	548 488G>A	R163H
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	550 490A>G	K164E
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	586 526C>T	R176C
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	586 526C>T	R176C
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	743 683G>A	F
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	785 725G>A	R242Q

K00396	K00396	107741	GEN-P0	(epsilon 2 and 3 alleles) mRNA	796 736C>T	R246C
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	821 761T>A	V254E
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	865 805C>G	R269G
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	935 875G>A	R292H
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	1000 940A>C	S314R
K00557	K00557	602529	GEN-TY	human alpha-tubulin mRNA, 3 end	126 126G>C	S
K01911	K01911	162640	GEN-2O	Neuropeptide Y	236 150G>A	S
K01911	K01911	162640	GEN-2O	Neuropeptide Y	290 204C>T	S
AGT	K02215	106150	GEN-WK	Human angiotensinogen mRNA, complete CDS	659 620C>T	T207M
AGT	K02215	106150	GEN-WK	Human angiotensinogen mRNA, complete CDS	842 803T>C	M268T
AGT	K02215	106150	GEN-WK	Human angiotensinogen mRNA, complete CDS	1155 1116G>A	S
AGT	K02215	106150	GEN-WK	Human angiotensinogen mRNA, complete CDS	1476 1437C>A	S
AGT	K02215	106150	GEN-WK	Human angiotensinogen mRNA, complete CDS	1821 1782G>A	3
AGT	K02215	106150	GEN-WK	Human angiotensinogen mRNA, complete CDS	2053 2014A>C	3
KNG	K02566	228960	GEN-X2	Human alpha-2-thiol proteinase inhibitor mRNA, complete coding sequence	1248 1199C>A	T400K
K02770	K02770	147720	GEN-5M	Interleukin 1, beta	19 (-68)A>C	5
K02770	K02770	147720	GEN-5M	Interleukin 1, beta	26 (-61)A>C	5
K02770	K02770	147720	GEN-5M	Interleukin 1, beta	48 (-39)C>T	5
K02770	K02770	147720	GEN-5M	Interleukin 1, beta	114 28G>A	E10K

K02770	K02770	147720	GEN-5M	Interleukin 1, beta	119 33G>A	M11I
L03558	L03558	601145	GEN-11O	Homo sapiens cystatin B mRNA, complete cds	485 390A>G	3
L05597	L05597	None	GEN-4EV	Serotonin 5-HT receptors 5-HT1F	824 600T>C	S
L05597	L05597	None	GEN-4EV	Serotonin 5-HT receptors 5-HT1F	1010 786^787insA [H262Q;26 ATAAATTC 2^263insl AT KFI]	5
EDNRB	L06623	131244	GEN-19S	Endothelin Receptor Type B	88 (-146)A>G	5
EDNRB	L06623	131244	GEN-19S	Endothelin Receptor Type B	332 99C>T	S
EDNRB	L06623	131244	GEN-19S	Endothelin Receptor Type B	1064 831G>A	S
EDNRB	L06623	131244	GEN-19S	Endothelin Receptor Type B	1064 831G>A	S
TGFBR3	L07594	600742	GEN-1EA	Human transforming growth factor-beta type III receptor (TGF-beta) mRNA, complete cds	3966 3618G>C	3
L07861	L07861	176977	GEN-D0	Protein kinase C, delta	445 387G>A	S
L07861	L07861	176977	GEN-D0	Protein kinase C, delta	1835 1777G>A	V593M
GNRHR	L07949	138850	GEN-1F1	Gonadotropin releasing hormone agonist	1371 1347C>A	3
CCKBR	L08112	118445	GEN-1FL	Cholecystokinin (CCKb)	456 456G>A	S
L08485	L08485	137142	GEN-G	Gamma-aminobutyric acid (GABA) A receptor, alpha 5	1646 1341G>T	S
L08485	L08485	137142	GEN-G	Gamma-aminobutyric acid (GABA) A receptor, alpha 5	2113 1808C>T	3
INPP1	L08488	147263	GEN-1FY	Human inositol polyphosphate 1-phosphatase mRNA, complete cds	185 (-142)T>G	5
INPP1	L08488	147263	GEN-1FY	Human inositol polyphosphate 1-phosphatase mRNA, complete cds	479 153T>G	S
INPP1	L08488	147263	GEN-	Human inositol polyphosphate 1-phosphatase mRNA, complete cds	674 348A>G	S

INPP1	L08488	147263	GEN-1FY	polyphosphate 1-phosphatase mRNA, complete cds	806 480G>A	S
MIF	L10612	153620	GEN-1J8	Human inositol polyphosphate 1-phosphatase mRNA, complete cds	170 96C>G	S
MIF	L10612	153620	GEN-1J8	Human glycosylation-inhibiting factor mRNA, complete cds	221 147C>G	S
MIF	L10612	153620	GEN-1J8	Human glycosylation-inhibiting factor mRNA, complete cds	227 153C>G	S
MIF	L10612	153620	GEN-1J8	Human glycosylation-inhibiting factor mRNA, complete cds	239 165G>A	S
MIF	L10612	153620	GEN-1J8	Human glycosylation-inhibiting factor mRNA, complete cds	329 255C>A	S
MIF	L10612	153620	GEN-1J8	Human glycosylation-inhibiting factor mRNA, complete cds	445 371C>T	3
L10819	L10819	171150	GEN-LVD	complete cds	191 153C>T	S
L10819	L10819	171150	GEN-LVD	Homo sapiens aryl sulfotransferase mRNA, complete cds	200 162G>A	S
L10819	L10819	171150	GEN-LVD	Homo sapiens aryl sulfotransferase mRNA, complete cds	230 192T>C	S
L10819	L10819	171150	GEN-LVD	Homo sapiens aryl sulfotransferase mRNA, complete cds	242 204G>A	S
L10819	L10819	171150	GEN-LVD	complete cds	295 257C>T	A86V
L10819	L10819	171150	GEN-LVD	Homo sapiens aryl sulfotransferase mRNA, complete cds	330 292G>A	D98N

L10819	L10819	L10819	L171150	GEN-LVD	sulfotransferase mRNA, complete cds Homo sapiens aryl sulfotransferase mRNA,	338 300G>A	S
L10819	L10819	L10819	L171150	GEN-LVD	Homo sapiens aryl sulfotransferase mRNA, complete cds	638 600C>G	S
L10819	L10819	L10819	L171150	GEN-LVD	Homo sapiens aryl sulfotransferase mRNA, complete cds	676 638A>G	H213R
L10819	L10819	L10819	L171150	GEN-LVD	Homo sapiens aryl sulfotransferase mRNA, complete cds	940 902G>A	3
L10819	L10819	L10819	L171150	GEN-LVD	Homo sapiens aryl sulfotransferase mRNA, complete cds	1011 973T>C	3
L11005	L11005	L11005	602841	GEN-1JU	Human aldehyde oxidase (hAOX) mRNA, complete cds	4284 4154C>A	3
L11005	L11005	L11005	602841	GEN-1JU	Human aldehyde oxidase (hAOX) mRNA, complete cds	4447 4317G>C	3
L11005	L11005	L11005	602841	GEN-1JU	Human aldehyde oxidase (hAOX) mRNA, complete cds	4525 4395T>G	3
L11005	L11005	L11005	602841	GEN-1JU	Human aldehyde oxidase (hAOX) mRNA, complete cds	4675 4545G>A	3
L11667	L11667	L11667	601753	GEN-H	Cyclophilin D 40kDa	1003 904C>A	L302I
L11667	L11667	L11667	601753	GEN-H	Cyclophilin D 40kDa	1283 1184A>G	3
L11667	L11667	L11667	601753	GEN-H	Cyclophilin D 40kDa	1479 1380T>A	3
L11667	L11667	L11667	601753	GEN-H	Cyclophilin D 40kDa	1519 1420T>C	3
L11931	L11931	L11931	182144	GEN-4DT	Human cytosolic serine hydroxymethyltransferase (SHMT) mRNA, complete cds	1444 1420C>T	L474F
L11931	L11931	L11931	182144	GEN-4DT	Human cytosolic serine hydroxymethyltransferase (SHMT) mRNA, complete cds	1541 1517C>T	3

L12052	L12052	171885	GEN-1LK	Human cAMP phosphodiesterase mRNA, 3 end	1707 1707G>A	3
L13266	L13266	138249	GEN-J	Glutamate Aspartate receptor NMDA 1	1618 525G>C	S
L13266	L13266	138249	GEN-J	Glutamate Aspartate receptor NMDA 1	1792 699C>A	S
L13266	L13266	138249	GEN-J	Glutamate Aspartate receptor NMDA 1	1948 855G>A	S
L13266	L13266	138249	GEN-J	Glutamate Aspartate receptor NMDA 1	2713 1620T>G	I540M
L13266	L13266	138249	GEN-J	Glutamate Aspartate receptor NMDA 1	3137 2044G>T	A682S
L13266	L13266	138249	GEN-J	Glutamate Aspartate receptor NMDA 1	3241 2148G>A	S
MDCR	L13385	601545	GEN-1O6	Glutamate Aspartate receptor NMDA 1 Homo sapiens(clone 71) Miller-Dieker lissencephaly protein (LIS1) mRNA, complete cds	1467 1250C>T	3
MDCR	L13385	601545	GEN-1O6	Homo sapiens(clone 71) Miller-Dieker lissencephaly protein (LIS1) mRNA, complete cds	1868 1651C>T	3
MDCR	L13385	601545	GEN-1O6	Homo sapiens(clone 71) Miller-Dieker lissencephaly protein (LIS1) mRNA, complete cds	1917 1700C>T	3
MDCR	L13385	601545	GEN-1O6	Homo sapiens(clone 71) Miller-Dieker lissencephaly protein (LIS1) mRNA, complete cds	2962 2745G>T	3
MDCR	L13385	601545	GEN-1O6	Homo sapiens(clone 71) Miller-Dieker lissencephaly protein (LIS1) mRNA, complete cds	4589 4372G>A	3
L13436	L13436	108961	GEN-2Q	guanylate cyclase	2222 2223C>T	3
L13436	L13436	108961	GEN-2Q	guanylate cyclase	2444 2445C>T	3
L13977	L13977	176785	GEN-1PX	Human prolylcarboxypeptidase mRNA, complete cds	2009 1980T>C	3
CAMK4	L17000	114080	GEN-	Homo sapiens	1381 1340C>T	A447V

1Zr	calcium/calmodulin-dependent protein kinase mRNA, complete cds										
L17075	PRKCI	L17075	601284	L17075	601284	GEN-1ZQ	Human TGF- β superfamily receptor type I mRNA, complete cds	838	747G>A	S	
L19760	PRKCI	L18964	300094	L18964	300094	GEN-21N	Human protein kinase C ι isoform (PRKCI) mRNA, complete cds	573	309T>G	S	
L19760		L19760	600322	L19760	600322	GEN-22D	Human nerve-terminal protein (isoform SNAP25A) mRNA, complete cds	259	171C>G	S	
L19760		L19760	600322	L19760	600322	GEN-22D	Human nerve-terminal protein (isoform SNAP25A) mRNA, complete cds	418	330T>C	S	
L19760		L19760	600322	L19760	600322	GEN-22D	Human nerve-terminal protein (isoform SNAP25A) mRNA, complete cds	629	541A>T	I181F	
L19956		L19956	600641	L19956	600641	GEN-LVE	Human aryl sulfotransferase mRNA, complete cds	243	105A>G	S	
L19956		L19956	600641	L19956	600641	GEN-LVE	Human aryl sulfotransferase mRNA, complete cds	284	146C>T	S49F	
HD		L20431	143100	L20431	143100	GEN-23G	Homo sapiens Huntington disease-associated protein (HD) mRNA, complete cds	1536	1535T>G	I512S	
HD		L20431	143100	L20431	143100	GEN-23G	Homo sapiens Huntington disease-associated protein (HD) mRNA, complete cds	2112	2111C>G	3	
HD		L20431	143100	L20431	143100	GEN-23G	Homo sapiens Huntington disease-associated protein (HD) mRNA, complete cds	3788	3787G>A	3	
HD		L20431	143100	L20431	143100	GEN-23G	Homo sapiens Huntington disease-associated protein (HD) mRNA, complete cds	4912	4911G>A	3	
HD		L20431	143100	L20431	143100	GEN-23G	Homo sapiens Huntington disease-associated protein (HD) mRNA, complete cds	5454	5453C>T	3	
L20463		L20463	600445	L20463	600445	GEN-M	G-protein coupled adenosine A3 receptor	1671	1380A>G	3	

VLDLR	L20470	192977	GEN-23D	Human very low density lipoprotein receptor mRNA, complete cds	336 (-56)C>T	5
VLDLR	L20470	192977	GEN-23D	Human very low density lipoprotein receptor mRNA, complete cds	3566 3175T>C	3
SOAT	L21934	102642	GEN-25C	Human acyl coenzyme A:cholesterol acyltransferase mRNA, complete cds	676 (-721)T>G	5
SOAT	L21934	102642	GEN-25C	Human acyl coenzyme A:cholesterol acyltransferase mRNA, complete cds	814 (-583)C>T	5
SOAT	L21934	102642	GEN-25C	Human acyl coenzyme A:cholesterol acyltransferase mRNA, complete cds	1993 597C>T	S
SOAT	L21934	102642	GEN-25C	Human acyl coenzyme A:cholesterol acyltransferase mRNA, complete cds	2365 969C>T	S
SOAT	L21934	102642	GEN-25C	Human acyl coenzyme A:cholesterol acyltransferase mRNA, complete cds	2821 1425G>C	S
SOAT	L21934	102642	GEN-25C	Human acyl coenzyme A:cholesterol acyltransferase mRNA, complete cds	3537 2141T>C	3
L22214	L22214	102775	GEN-2S	Adenosine A1 receptor (ADORA1)	557 147G>C	S
L22214	L22214	102775	GEN-2S	Adenosine A1 receptor (ADORA1)	2622 2212G>A	3
SLC6A3	L24178	126455	GEN-283	Homo sapiens dopamine transporter mRNA, complete cds	1917 1898C>T	3
L24470	L24470	600563	GEN-O	PROSTAGLANDIN F RECEPTOR	1422 1185T>C	3
L24470	L24470	600563	GEN-O	PROSTAGLANDIN F RECEPTOR	1490 1253C>T	3

L24470	L24470	600563	GEN-O	PROSTAGLANDIN F RECEPTOR	1517 1280A>G	3
L24470	L24470	600563	GEN-O	PROSTAGLANDIN F RECEPTOR	2244 2007A>G	3
L24470	L24470	600563	GEN-O	PROSTAGLANDIN F RECEPTOR	2299 2062A>G	3
OPRM1	L25119	600018	GEN- 4EP	Human Mu opiate receptor (MOR1) mRNA, complete cds	41 (-172)G>T	5
OPRM1	L25119	600018	GEN- 4EP	Human Mu opiate receptor (MOR1) mRNA, complete cds	102 (-111)C>T	5
OPRM1	L25119	600018	GEN- 4EP	Human Mu opiate receptor (MOR1) mRNA, complete cds	229 17C>T	A6V
OPRM1	L25119	600018	GEN- 4EP	Human Mu opiate receptor (MOR1) mRNA, complete cds	229 17C>T	A6V
OPRM1	L25119	600018	GEN- 4EP	Human Mu opiate receptor (MOR1) mRNA, complete cds	236 24G>A	S
OPRM1	L25119	600018	GEN- 4EP	Human Mu opiate receptor (MOR1) mRNA, complete cds	330 118A>G	N40D
OPRM1	L25119	600018	GEN- 4EP	Human Mu opiate receptor (MOR1) mRNA, complete cds	330 118A>G	N40D
OPRM1	L25119	600018	GEN- 4EP	Human Mu opiate receptor (MOR1) mRNA, complete cds	991 779G>A	R260H
OPRM1	L25119	600018	GEN- 4EP	Human Mu opiate receptor (MOR1) mRNA, complete cds	1005 793C>T	R265C
OPRM1	L25119	600018	GEN- 4EP	Human Mu opiate receptor (MOR1) mRNA, complete cds	1154 942G>A	S
OPRM1	L25119	600018	GEN- 4EP	Human Mu opiate receptor (MOR1) mRNA, complete cds	1154 942G>A	S
L26232	L26232	172425	GEN- 2AK	Human phospholipid transfer protein mRNA, cds	906 819C>T	S

L26232	L26232	172425	GEN-2AK	complete cds Human phospholipid transfer protein mRNA,	1547 1460C>A	T487K
PTGER2	L28175	601586	GEN-7C	complete cds Prostaglandin E receptor 2 (subtype EP2), 53kD	547 159C>T	S
PTGER2	L28175	601586	GEN-7C	Prostaglandin E receptor 2 (subtype EP2), 53kD	611 223G>A	V75M
PTGER2	L28175	601586	GEN-7C	Prostaglandin E receptor 2 (subtype EP2), 53kD	1725 1337A>G	Q446R
L31773	L31773	104220	GEN-4DD	Adrenergic receptor alpha 1b	171 171C>T	S
L31773	L31773	104220	GEN-4DD	Adrenergic receptor alpha 1b	534 534C>T	S
L31773	L31773	104220	GEN-4DD	Adrenergic receptor alpha 1b	549 549G>A	S
L33798	L33798	114208	GEN-Q	Ca Channel alpha1s L-Type	5667 5442C>G	S
L33798	L33798	114208	GEN-Q	Ca Channel alpha1s L-Type	5669 5444G>C	G1815A
L33798	L33798	114208	GEN-Q	Ca Channel alpha1s L-Type	5745 5520C>G	D1840E
L33798	L33798	114208	GEN-Q	Ca Channel alpha1s L-Type	5941 5716C>A	3
L33798	L33798	114208	GEN-Q	Ca Channel alpha1s L-Type	5971 5746C>A	3
L33798	L33798	114208	GEN-Q	Ca Channel alpha1s L-Type	5985 5760G>A	3
L36151	L36151	600286	GEN-DT	PHOSPHATIDYLINOSITO L4-KINASE ALPHA	1857 1740C>T	S
L36151	L36151	600286	GEN-DT	PHOSPHATIDYLINOSITO L4-KINASE ALPHA	2052 1935C>T	S
L36151	L36151	600286	GEN-DT	PHOSPHATIDYLINOSITO L4-KINASE ALPHA	2160 2043T>C	S
L36151	L36151	600286	GEN-DT	PHOSPHATIDYLINOSITO L4-KINASE ALPHA	2280 2163T>C	S
L36151	L36151	600286	GEN-DT	PHOSPHATIDYLINOSITO L4-KINASE ALPHA	2644 2527G>A	D843N
L36151	L36151	600286	GEN-DT	PHOSPHATIDYLINOSITO L4-KINASE ALPHA	2749 2632C>A	3
L36151	L36151	600286	GEN-DT	PHOSPHATIDYLINOSITO L4-KINASE ALPHA	2799 2682A>G	3

L36151	L36151	600286	GEN-DT	L 4-KINASE ALPHA PHOSPHATIDYLINOSITO	2804	2687A>G	3
L36151	L36151	600286	GEN-DT	L 4-KINASE ALPHA PHOSPHATIDYLINOSITO	2844	2727C>G	3
L36151	L36151	600286	GEN-DT	L 4-KINASE ALPHA PHOSPHATIDYLINOSITO	2848	2731G>A	3
L36151	L36151	600286	GEN-DT	L 4-KINASE ALPHA PHOSPHATIDYLINOSITO	2857	2740A>G	3
L36151	L36151	600286	GEN-DT	L 4-KINASE ALPHA PHOSPHATIDYLINOSITO	2877	2760A>G	3
L36151	L36151	600286	GEN-DT	L 4-KINASE ALPHA PHOSPHATIDYLINOSITO	2942	2825C>T	3
L36566	L36566	601970	GEN- 2N5	L 4-KINASE ALPHA Human helodermin- preferring VIP receptor (VIP2/PACAP receptor) mRNA, complete cds	1397	1235A>G	H412R
L36566	L36566	601970	GEN- 2N5	Human helodermin- preferring VIP receptor (VIP2/PACAP receptor) mRNA, complete cds	1440	1278A>C	S
L37792	L37792	186590	GEN-DX	mRNA, complete cds	1337	1336A>G	3
L41147	L41147	601109	GEN-2T	serotonin 1A 5-HT6	287	(-181)C>T	5
L42373	L42373	601643	GEN- 2U7	Homo sapiens phosphatase 2A B56-alpha (PP2A) mRNA, complete cds	1135	564C>T	S
L42373	L42373	601643	GEN- 2U7	Homo sapiens phosphatase 2A B56-alpha (PP2A) mRNA, complete cds	2297	1726T>A	3
L42373	L42373	601643	GEN- 2U7	Homo sapiens phosphatase 2A B56-alpha (PP2A) mRNA, complete cds	2368	1797T>C	3
L42373	L42373	601643	GEN- 2U7	Homo sapiens phosphatase 2A B56-alpha (PP2A) mRNA, complete cds	2782	2211G>A	3
L42373	L42373	601643	GEN- 2U7	Homo sapiens phosphatase 2A B56-alpha (PP2A) mRNA, complete cds	2952	2381T>G	3

SD-144146.1

HEXB	M13519	268800	GEN-10I	glucosaminidase (HEXB) mRNA, 3 end	490 490T>G	S164A
HEXB	M13519	268800	GEN-10I	Human N-acetyl-beta-glucosaminidase (HEXB) mRNA, 3 end	1741 1741A>C	3
HEXB	M13519	268800	GEN-10I	Human N-acetyl-beta-glucosaminidase (HEXB) mRNA, 3 end	1798 1798A>G	3
M14113 DBI	M14113 M14200	306700 125950	GEN-5T GEN-1QW	Human N-acetyl-beta-glucosaminidase (HEXB) mRNA, 3 end Factor VIII Human diazepam binding inhibitor (DBI) mRNA, complete cds	8899 8728G>A 291 272A>T	3 Y91F
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	184 (-11)T>C	5
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	270 76G>C	V26L
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	446 252C>T	S
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1254 1060C>G	3
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1306 1112G>A	3
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1336 1142T>A	3
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1338 1144C>T	3
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1451 1257G>A	3
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1462 1268C>T	3

M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1522 1328G>C	3
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1557 1363G>C	3
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1585 1391C>A	3
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1630 1436T>C	3
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1668 1474T>G	3
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1712 1518C>G	3
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1898 1704A>G	3
M14333	M14333	137025	GEN-QO	Homo sapiens c-syn protooncogene mRNA, complete cds	562 (-18)A>C	5
M14333	M14333	137025	GEN-QO	Homo sapiens c-syn protooncogene mRNA, complete cds	1647 1068T>C	S
M14333	M14333	137025	GEN-QO	Homo sapiens c-syn protooncogene mRNA, complete cds	2152 1573A>T	T525S
ARG1	M14502	207800	GEN- 1RE	Human liver arginase mRNA, complete cds	800 744C>T	S
M14539	M14539	134570	GEN-QP	Human factor XIII subunit a mRNA, 3 end	1781 1781C>T	P594L
M14539	M14539	134570	GEN-QP	Human factor XIII subunit a mRNA, 3 end	2041 2041C>G	Q681E
M14539	M14539	134570	GEN-QP	Human factor XIII subunit a mRNA, 3 end	2412 2412C>T	3
M14539	M14539	134570	GEN-QP	Human factor XIII subunit a mRNA, 3 end	2446 2446G>A	3

M14539	M14539	134570	GEN-QP	Human factor XIII subunit a mRNA, 3 end	3282 3282G>T	3
NGFR	M14764	162010	GEN-1S8	Human nerve growth factor receptor mRNA, complete cds	2716 2603C>T	3
NGFR	M14764	162010	GEN-1S8	Human nerve growth factor receptor mRNA, complete cds	2729 2616C>T	3
NGFR	M14764	162010	GEN-1S8	Human nerve growth factor receptor mRNA, complete cds	2912 2799G>A	3
NGFR	M14764	162010	GEN-1S8	Human nerve growth factor receptor mRNA, complete cds	3252 3139C>G	3
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	466 (-1122)C>G	5
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	565 (-1023)G>A	5
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	1541 (-47)C>T	5
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	1633 46A>G	R16G
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	1633 46A>G	R16G
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	1666 79C>G	Q27E
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	1666 79C>G	Q27E
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	1666 79C>G	Q27E
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	1687 100G>A	V34M
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	1839 252G>A	S
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	2110 523C>A	S
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	2640 1053G>C	S
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	2826 1239G>A	S
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	2862 1275C>G	3
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	2864 1277C>A	3
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	2865 1278C>A	3
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	3371 1784A>T	3
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	422 293A>G	D98G
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	557 428G>A	G143D
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	564 435-436TT>AG>A	F146V
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	568 439C>T	F
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	596 467A>G	Y156C

M16541	M16541	177400	GEN-35	Butyrylcholinesterase	941 812C>T	T271M
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	961 832A>C	T278P
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	978 849G>C	E283D
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1201 1072T>A	L358I
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1306 1177G>A	G393R
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1382 1253G>T	G418V
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1549 1420T>G	F474V
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1564 1435G>T	F
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1703 1574A>T	E525V
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1756 1627C>T	R543C
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1828 1699G>A	A567T
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1828 1699G>A	A567T
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	2127 1998A>G	3
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	2127 1998A>G	3
M16765	M16765	104760	GEN-1YM	Human cerebrovascular and neuritic plaque amyloid beta-protein mRNA, 3 end	1283 1274A>C	3
F5	M16967	227400	GEN-1Z8	Human coagulation factor V mRNA, complete cds	2391 2301G>A	S
F5	M16967	227400	GEN-1Z8	Human coagulation factor V mRNA, complete cds	2663 2573G>A	R858K
F5	M16967	227400	GEN-1Z8	Human coagulation factor V mRNA, complete cds	2684 2594G>A	R865H
F5	M16967	227400	GEN-1Z8	Human coagulation factor V mRNA, complete cds	5380 5290G>A	V1764M
CYP21	M17252	201910	GEN-201	Human cytochrome P450c21 mRNA, 3 end	224 224G>A	R75H
CYP21	M17252	201910	GEN-201	Human cytochrome P450c21 mRNA, 3 end	330 330C>T	S
CYP21	M17252	201910	GEN-201	Human cytochrome P450c21 mRNA, 3 end	745 745T>C	3
M17262	M17262	176930	GEN-SM	Human prothrombin (F2) gene, complete cds, and Alu and KpnI repeats	511 480C>T	S
M20132	M20132	313700	GEN-38	Androgen receptor (dihydrotestosterone receptor)	995 633G>A	S
M20132	M20132	313700	GEN-38	Androgen receptor	1385 1023T>C	S

M20132	M20132	313700	GEN-38	(dihydrotestosterone receptor)	1786 1424G>A	G475E
M21054	M21054	172410	GEN-3B	Androgen receptor (dihydrotestosterone receptor)	331 294G>A	S
M21054	M21054	172410	GEN-3B	Phospholipase A-2 (PLA-2) lung	400 363C>A	D121E
M21551	M21551	162340	GEN-24P	Human neuromedin B mRNA, complete cds	252 216C>A	S
PLA2G2A	M22430	172411	GEN-25V	Human RASF-A PLA2 mRNA, complete cds	116 (-20)G>T	5
PLA2G2A	M22430	172411	GEN-25V	Human RASF-A PLA2 mRNA, complete cds	231 96G>C	S
PLA2G2A	M22430	172411	GEN-25V	Human RASF-A PLA2 mRNA, complete cds	267 132C>T	S
PLA2G2A	M22430	172411	GEN-25V	Human RASF-A PLA2 mRNA, complete cds	267 132C>T	S
PLA2G2A	M22430	172411	GEN-25V	Human RASF-A PLA2 mRNA, complete cds	278 143-144GT>GT	S
PLA2G2A	M22430	172411	GEN-25V	Human RASF-A PLA2 mRNA, complete cds	278 143-144delGT	F
PLA2G2A	M22430	172411	GEN-25V	Human RASF-A PLA2 mRNA, complete cds	643 508C>T	3
PLA2G2A	M22430	172411	GEN-25V	Human RASF-A PLA2 mRNA, complete cds	700 565G>C	3
M22538	M22538	600532	GEN-EO	NADH dehydrogenase (ubiquinone) flavoprotein 2 (24kD)	219 201A>T	S
M22538	M22538	600532	GEN-EO	NADH dehydrogenase (ubiquinone) flavoprotein 2 (24kD)	469 451G>A	A151T
M22613	M22613	227600	GEN-3C	COAGULATION FACTOR X PRECURSOR	738 738C>T	S
M22632	M22632	138150	GEN-EP	Glutamic-oxaloacetic transaminase 2, mitochondrial (aspartate aminotransferase 2)	221 213T>C	S
M22632	M22632	138150	GEN-EP	Glutamic-oxaloacetic transaminase 2	236 228T>G	S

M22632	M22632	138150	GEN-EP	mitochondrial (aspartate aminotransferase 2)	2009 2001C>T	3
M24194	M24194	None	GEN-286	Glutamic-oxaloacetic transaminase 2, mitochondrial (aspartate aminotransferase 2)	79 (-17)C>A	5
M24194	M24194	None	GEN-286	Human MHC protein homologous to chicken B complex protein mRNA, complete cds	102 7G>T	F
M24194	M24194	None	GEN-286	Human MHC protein homologous to chicken B complex protein mRNA, complete cds	464 369A>T	S
M24194	M24194	None	GEN-286	Human MHC protein homologous to chicken B complex protein mRNA, complete cds	846 751G>T	A251S
M24194	M24194	None	GEN-286	Human MHC protein homologous to chicken B complex protein mRNA, complete cds	848 753C>T	S
M24857	M24857	180190	GEN-80	Retinoic acid receptor, gamma 1	1694 1280C>T	S427L
CRYAB	M24906	123590	GEN-28V	Homo sapiens Rosenthal fiber protein (alpha-B-crystallin) mRNA, 3 end	107 107T>G	V36G
CRYAB	M24906	123590	GEN-28V	Homo sapiens Rosenthal fiber protein (alpha-B-crystallin) mRNA, 3 end	303 303A>T	3
CRYAB	M24906	123590	GEN-28V	Homo sapiens Rosenthal fiber protein (alpha-B-crystallin) mRNA, 3 end	305 305G>A	3
GAP43	M25667	162060	GEN-29U	Human neuronal growth protein 43 (GAP-43) mRNA, complete cds	1086 995T>G	3
M25756	M25756	118930	GEN-	Human secretogranin II	855 793G>A	V265M

M2756	M2756	118930	29W GEN- 29W GEN-3E	gene, complete cds Human secretogranin II gene, complete cds	899 837C>T	S
M26383	M26383	146930	GEN-3E	Interleukin 8	259 185C>G	A62G
M26383	M26383	146930	GEN-3E	Interleukin 8	1237 1163A>T	3
M26383	M26383	146930	GEN-3E	Interleukin 8	1281 1207A>G	3
M27436	M27436	134390	GEN-R7	Human tissue factor gene, complete cds, with a Alu repetitive sequence in the 3 untranslated region	1414 1315C>T	3
M27436	M27436	134390	GEN-R7	Human tissue factor gene, complete cds, with a Alu repetitive sequence in the 3 untranslated region	1508 1409A>G	3
M27436	M27436	134390	GEN-R7	Human tissue factor gene, complete cds, with a Alu repetitive sequence in the 3 untranslated region	1588 1489T>G	3
M27492	M27492	147810	GEN-3F	3 untranslated region INTERLEUKIN 1 RECEPTOR, TYPE I PRECURSOR	4686 4604T>G	3
M27875	M27875	107680	GEN- 2CK	Human apolipoprotein A-I mRNA, complete cds	34 15G>C	S
M27875	M27875	107680	GEN- 2CK	Human apolipoprotein A-I mRNA, complete cds	202 183C>T	S
M27875	M27875	107680	GEN- 2CK	Human apolipoprotein A-I mRNA, complete cds	204 185T>G	L62W
M27875	M27875	107680	GEN- 2CK	Human apolipoprotein A-I mRNA, complete cds	255 236C>T	S79F
M27875	M27875	107680	GEN- 2CK	Human apolipoprotein A-I mRNA, complete cds	689 670C>T	S
M27875	M27875	107680	GEN- 2CK	Human apolipoprotein A-I mRNA, complete cds	824 805G>A	3
M28211	M28211	179511	GEN- 2D1	Human apolipoprotein A-I mRNA, complete cds Homo sapiens GTP- binding protein (RAB4)	677 607A>G	T203A
M28211	M28211	179511	GEN- 2D1	mRNA, complete cds Homo sapiens GTP- binding protein (RAB4)	679 609C>A	S
M28215	M28215	179512	GEN- 2D3	mRNA, complete cds Homo sapiens GTP- binding protein (RAB5)	297 241G>C	G81R

POMC	M28636	178830	GEN-2DG	mRNA, complete cds Adrenocorticotrophic hormone (ACTH)	92 92C>T	3
CETP	M30185	118470	GEN-2FK	Human cholesteryl ester transfer protein mRNA, complete cds	1283 1153G>C	V385L
CETP	M30185	118470	GEN-2FK	Human cholesteryl ester transfer protein mRNA, complete cds	1298 1168G>C	A390P
CETP	M30185	118470	GEN-2FK	Human cholesteryl ester transfer protein mRNA, complete cds	1394 1264A>G	I422V
CETP	M30185	118470	GEN-2FK	Human cholesteryl ester transfer protein mRNA, complete cds	1394 1264A>G	I422V
CETP	M30185	118470	GEN-2FK	Human cholesteryl ester transfer protein mRNA, complete cds	1506 1376A>G	D459G
CETP	M30185	118470	GEN-2FK	Human cholesteryl ester transfer protein mRNA, complete cds	1696 1566G>A	3
M30262	M30262	600295	GEN-WA	Human cardiolipin-atrial natriuretic factor (CDD-ANF) mRNA, complete cds	178 79C>T	P27S
M30262	M30262	600295	GEN-WA	Human cardiolipin-atrial natriuretic factor (CDD-ANF) mRNA, complete cds	203 104C>G	A35G
M30262	M30262	600295	GEN-WA	Human cardiolipin-atrial natriuretic factor (CDD-ANF) mRNA, complete cds	210 111G>T	S
M30262	M30262	600295	GEN-WA	Human cardiolipin-atrial natriuretic factor (CDD-ANF) mRNA, complete cds	327 228C>T	S
M30262	M30262	600295	GEN-WA	Human cardiolipin-atrial natriuretic factor (CDD-ANF) mRNA, complete cds	553 454T>C	F
M30262	M30262	600295	GEN-WA	Human cardiolipin-atrial natriuretic factor (CDD-ANF) mRNA, complete cds	626 527G>T	3
M30262	M30262	600295	GEN-WA	Human cardiolipin-atrial natriuretic factor (CDD-ANF) mRNA, complete cds	640 541T>C	3

M31328	M31328	139130	GEN-7G	ANF) mRNA, complete cds	1049 1043G>A	3
M32313	M32313	184753	GEN-5Y	Guanine nucleotide binding protein (G protein), beta polypeptide 3	1271 1241C>T	3
M32313	M32313	184753	GEN-5Y	Steroid 5 alpha reductase 1	1344 1314G>A	3
M32313	M32313	184753	GEN-5Y	Steroid 5 alpha reductase 1	1489 1459G>A	3
M32313	M32313	184753	GEN-5Y	Steroid 5 alpha reductase 1	1780 1750T>C	3
M32315	M32315	191191	GEN-3M	Tumor necrosis factor receptor 2 (75kD)	676 587T>G	M196R
M32315	M32315	191191	GEN-3M	Tumor necrosis factor receptor 2 (75kD)	1176 1087G>A	A363T
M32315	M32315	191191	GEN-3M	Tumor necrosis factor receptor 2 (75kD)	1668 1579G>T	3
M32315	M32315	191191	GEN-3M	Tumor necrosis factor receptor 2 (75kD)	2898 2809G>A	3
M32315	M32315	191191	GEN-3M	Tumor necrosis factor receptor 2 (75kD)	3671 3582G>A	3
M34479	M34479	179060	GEN-F9	Pyruvate dehydrogenase (lipoamide) beta	109 109G>A	D37N
M34479	M34479	179060	GEN-F9	Pyruvate dehydrogenase (lipoamide) beta	438 438A>G	S
M34479	M34479	179060	GEN-F9	Pyruvate dehydrogenase (lipoamide) beta	1172 1172A>C	3
M34479	M34479	179060	GEN-F9	Pyruvate dehydrogenase (lipoamide) beta	1179 1179C>T	3
M34479	M34479	179060	GEN-F9	Pyruvate dehydrogenase (lipoamide) beta	1323 1323C>A	3
M34479	M34479	179060	GEN-F9	Pyruvate dehydrogenase (lipoamide) beta	1376 1376G>C	3
M34479	M34479	179060	GEN-F9	Pyruvate dehydrogenase (lipoamide) beta	1433 1433C>T	3
M34539	M34539	186945	GEN-3N	FKBP, tacrolimus binding protein, FK506-binding protein 1 (12kD)	449 371A>G	3
M34539	M34539	186945	GEN-3N	FKBP, tacrolimus binding protein, FK506-binding protein	486 408G>A	3

M34539	M34539	186945	GEN-3N	protein 1 (12kD) FKBP, tacrolimus binding protein, FK506-binding protein 1 (12kD)	650 572T>C	3
M36035	M36035	109610	GEN-3P	Benzodiazepine receptor, peripheral-type	500 439G>A	A147T
M36035	M36035	109610	GEN-3P	Benzodiazepine receptor, peripheral-type	500 439G>A	A147T
M36035	M36035	109610	GEN-3P	Benzodiazepine receptor, peripheral-type	546 485A>G	H162R
M36035	M36035	109610	GEN-3P	Benzodiazepine receptor, peripheral-type	546 485A>G	H162R
M36035	M36035	109610	GEN-3P	Benzodiazepine receptor, peripheral-type	711 650T>G	3
M37400	M37400	138180	GEN-FC	Glutamic-oxaloacetic transaminase 1, soluble (aspartate aminotransferase 1)	1588 1564A>C	3
M37400	M37400	138180	GEN-FC	Glutamic-oxaloacetic transaminase 1, soluble (aspartate aminotransferase 1)	1810 1786G>A	3
M55040	M55040	100740	GEN-3Q	acetylcholinesterase	323 167C>T	P56L
M55040	M55040	100740	GEN-3Q	acetylcholinesterase	1154 998T>A	V333E
M55040	M55040	100740	GEN-3Q	acetylcholinesterase	1213 1057C>A	H353N
M55040	M55040	100740	GEN-3Q	acetylcholinesterase	1482 1326G>T	S
M55040	M55040	100740	GEN-3Q	acetylcholinesterase	1587 1431C>T	S
M55040	M55040	100740	GEN-3Q	acetylcholinesterase	1587 1431C>T	S
M55040	M55040	100740	GEN-3Q	acetylcholinesterase	1663 1507T>C	F503L
M57414	M57414	None	GEN-4FK	Human neurokinin A receptor (NK-2R) mRNA, complete cds	68 68T>C	I23T
M57414	M57414	None	GEN-4FK	Human neurokinin A receptor (NK-2R) mRNA, complete cds	951 951G>A	S
M57414	M57414	None	GEN-4FK	Human neurokinin A receptor (NK-2R) mRNA, complete cds	1171 1171C>G	P391A
M58525	M58525	116790	GEN-3S	Catechol-O- methyltransferase	390 186T>C	S

M58525	M58525	116790	GEN-3S	Catechol-O-methyltransferase	390 186T>C	S
M58525	M58525	116790	GEN-3S	Catechol-O-methyltransferase	418 214G>T	A72S
M58525	M58525	116790	GEN-3S	Catechol-O-methyltransferase	423 219G>A	S
M58525	M58525	116790	GEN-3S	Catechol-O-methyltransferase	612 408C>G	S
M58525	M58525	116790	GEN-3S	Catechol-O-methyltransferase	676 472A>G	M158V
M58525	M58525	116790	GEN-3S	Catechol-O-methyltransferase	676 472A>G	M158V
M58525	M58525	116790	GEN-3S	Catechol-O-methyltransferase	813 609C>T	S
M58525	M58525	116790	GEN-3S	Catechol-O-methyltransferase	1031 827delC	F
M58525	M58525	116790	GEN-3S	Catechol-O-methyltransferase	1039 835C>A	3
M59305	M59305	108962	GEN-39P	Human atrial natriuretic peptide clearance receptor (ANP C-receptor) mRNA, complete cds	160 (-203)-(-199)delTTTTT	F
M59979	M59979	176805	GEN-Z	Cyclooxygenase 1 COX1	644 639C>A	S
M59979	M59979	176805	GEN-Z	Cyclooxygenase 1 COX1	1892 1887C>A	3
M59979	M59979	176805	GEN-Z	Cyclooxygenase 1 COX1	2030 2025G>A	3
TCN2	M60396	275350	GEN-3AX	Human transcobalamin II (TCII) mRNA, complete cds	1164 1127C>T	S376L
TCN2	M60396	275350	GEN-3AX	Human transcobalamin II (TCII) mRNA, complete cds	1765 1728T>C	3
M60857	M60857	123841	GEN-10	Cyclophilin B	183 171C>T	S
M60857	M60857	123841	GEN-10	Cyclophilin B	217 205G>T	V69L
M60857	M60857	123841	GEN-10	Cyclophilin B	702 690C>T	3
M60857	M60857	123841	GEN-10	Cyclophilin B	804 792A>C	3
M62762	M62762	108745	GEN-FP	Vacuolar H+ ATPase proton channel subunit	425 195C>T	S
M62762	M62762	108745	GEN-FP	Vacuolar H+ ATPase proton channel subunit	784 554C>G	3
M62762	M62762	108745	GEN-FP	Vacuolar H+ ATPase proton channel subunit	838 608C>T	3

LRPAP1	M63959	104225	GEN-3EI	proton channel subunit Human alpha-2-macroglobulin receptor-associated protein mRNA, complete cds	850 837G>A	S
LRPAP1	M63959	104225	GEN-3EI	Human alpha-2-macroglobulin receptor-associated protein mRNA, complete cds	1093 1080C>T	3
LRPAP1	M63959	104225	GEN-3EI	Human alpha-2-macroglobulin receptor-associated protein mRNA, complete cds	1249 1236C>T	3
FGFR3	M64347	134934	GEN-3EX	Human novel growth factor receptor mRNA, 3 cds	3108 3108C>A	3
FGFR3	M64347	134934	GEN-3EX	Human novel growth factor receptor mRNA, 3 cds	3715 3715G>A	3
M64590	M64590	238300	GEN-FU	Glycine cleavage system: Protein P	3076 2926A>G	M976V
M64799	M64799	None	GEN-4DN	Histamine receptor H2	398 398T>C	V133A
M64799	M64799	None	GEN-4DN	Histamine receptor H2	525 525A>T	K175N
M64799	M64799	None	GEN-4DN	Histamine receptor H2	620 620A>G	K207R
M64799	M64799	None	GEN-4DN	Histamine receptor H2	649 649A>G	N217D
M64799	M64799	None	GEN-4DN	Histamine receptor H2	692 692A>G	K231R
M64799	M64799	None	GEN-4DN	Histamine receptor H2	802 802G>A	V268M
PRKAR1 B	M65066	176911	GEN-3FK	Human cAMP-dependent protein kinase regulatory subunit RI-beta mRNA, 3 end	1424 1424C>G	3
PRKAR1 B	M65066	176911	GEN-3FK	Human cAMP-dependent protein kinase regulatory subunit RI-beta mRNA, 3 end	1514 1514G>C	3
PRKAR1 B	M65066	176911	GEN-3FK	Human cAMP-dependent protein kinase regulatory subunit RI-beta mRNA, 3 end	1550 1550G>C	3

PRKAR1 B	M65066	176911	GEN-3FK	subunit RI-beta mRNA, 3 end	1862 1862G>A	3
PRKAR1 B	M65066	176911	GEN-3FK	Human cAMP-dependent protein kinase regulatory subunit RI-beta mRNA, 3 end	2139 2139C>T	3
FSHR	M65085	136435	GEN-3FQ	FSH receptor	2105 2039G>A	S680N
EDN2	M65199	131241	GEN-CBS	Endothelin 2	384 314C>T	A105V
EDN2	M65199	131241	GEN-CBS	Endothelin 2	997 927A>G	3
EDN2	M65199	131241	GEN-CBS	Endothelin 2	997 927A>G	3
M67439	M67439	126453	GEN-4EI	Dopamine Receptor D5	1500 1353T>A	S
M67439	M67439	126453	GEN-4EI	Dopamine Receptor D5	1512 1365G>A	F
M67439	M67439	126453	GEN-4EI	Dopamine Receptor D5	1566 1419G>A	S
M69175	M69175	238330	GEN-FX	Glycine cleavage system: Protein H	710 686C>G	3
M69175	M69175	238330	GEN-FX	Glycine cleavage system: Protein H	710 686C>G	3
M69175	M69175	238330	GEN-FX	Glycine cleavage system: Protein H	737 713C>T	3
M69175	M69175	238330	GEN-FX	Glycine cleavage system: Protein H	1007 983C>T	3
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	435 385A>C	S
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	936 886C>T	F
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	941 891T>G	S
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	941 891T>G	S
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	1076 1026A>T	S
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	1373 1323G>A	F
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	1460 1410C>T	S
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	1460 1410C>T	S
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	1609 1559A>G	K520R
SRD5A2	M74047	264600	GEN-	Human steroid 5-alpha-	2379 2352A>G	3

SD-144146.1

M83566	M83566	114206	GEN-3Y7	mRNA, complete cds Human neuroendocrine/beta-cell-type calcium channel alpha-1 subunit mRNA, complete cds	1222 1104C>T	S
M83566	M83566	114206	GEN-3Y7	Human neuroendocrine/beta-cell-type calcium channel alpha-1 subunit mRNA, complete cds	1468 1350G>A	S
CHRNA5	M83712	118505	GEN-3YQ	Nicotinic, Cholinergic receptor alpha 5	1340 1192G>A	D398N
M84755	M84755	162641	GEN-46	Neuropeptide Y1	1121 1121A>C	K374T
TGFBR2	M85079	190182	GEN-3ZS	Human TGF-beta type II receptor mRNA, complete cds	2045 1710A>C	3
YWHAZ	M86400	601288	GEN-40Y	Human phospholipase A2 mRNA, complete cds	1653 1569T>A	3
YWHAZ	M86400	601288	GEN-40Y	Human phospholipase A2 mRNA, complete cds	2599 2515C>G	3
YWHAZ	M86400	601288	GEN-40Y	Human phospholipase A2 mRNA, complete cds	2619 2535A>C	3
YWHAZ	M86400	601288	GEN-40Y	Human phospholipase A2 mRNA, complete cds	2656 2572A>C	3
YWHAZ	M86400	601288	GEN-40Y	Human phospholipase A2 mRNA, complete cds	2745 2661C>T	3
YWHAZ	M86400	601288	GEN-40Y	Human phospholipase A2 mRNA, complete cds	2761 2677A>C	3
GABRR2	M86868	137162	GEN-4FS	Gamma-aminobutyric acid (GABA) A receptor	1369 1289C>T	T430M
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	296 16T>C	S6P
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	413 133G>A	G45R
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	853 573T>C	S
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	853 573T>C	S
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	1342 1062A>G	S
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	1342 1062A>G	S
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	1430 1150T>G	3
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	1446 1166C>A	3

M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	1446 1166C>A	3
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	1446 1166C>A	3
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	1453 1173A>G	3
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	1677 1397G>A	3
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	1797 1517G>T	3
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	1885 1605C>T	3
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	1916 1636T>C	3
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	2158 1878A>G	3
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	1614 1471T>C	3
M89473	M89473	None	GEN-4FU	NEUROMEDIN K RECEPTOR		
M90100	M90100	600262	GEN-1A	Cyclooxygenase 2 COX2	2159 2062G>C	3
M90100	M90100	600262	GEN-1A	Cyclooxygenase 2 COX2	2186 2089-2094ATATTA	3
M90100	M90100	600262	GEN-1A	Cyclooxygenase 2 COX2	2186 2089->ATATTA	3
M90100	M90100	600262	GEN-1A	Cyclooxygenase 2 COX2	2094deATATTA	3
M90100	M90100	600262	GEN-1A	Cyclooxygenase 2 COX2	2230 2133A>G	3
M90100	M90100	600262	GEN-1A	Cyclooxygenase 2 COX2	2339 2242T>C	3
M90100	M90100	600262	GEN-1A	Cyclooxygenase 2 COX2	2409 2312G>A	3
M90100	M90100	600262	GEN-1A	Cyclooxygenase 2 COX2	2726 2629C>T	3
M90100	M90100	600262	GEN-1A	Cyclooxygenase 2 COX2	2983 2886C>T	3
M92269	M92269	114205	GEN-SV	Ca Channel alpha1c (alt. splice) L-Type	3846 3846C>T	S
M92269	M92269	114205	GEN-SV	Ca Channel alpha1c (alt. splice) L-Type	5505 5505G>A	S
M92269	M92269	114205	GEN-SV	Ca Channel alpha1c (alt. splice) L-Type	6582 6582A>G	S
M92269	M92269	114205	GEN-SV	Ca Channel alpha1c (alt. splice) L-Type	6613 6613G>C	G2205R
M92269	M92269	114205	GEN-SV	Ca Channel alpha1c (alt. splice) L-Type	6614 6614G>C	G2205A
M93415	M93415	102581	GEN-48S	Human activin type II receptor mRNA, complete cds	136 (-38)G>T	5
M94055	M94055	601219	GEN-493	Human voltage-gated sodium channel mRNA, complete cds	5226 5121G>A	S
IL8RB	M94582	146928	GEN-	Interleukin 8 receptor	838 786T>C	S

IL8RB	M94582	146928	49G GEN- 49G	Interleukin 8 receptor	1262 1210C>T	3
IL8RB	M94582	146928	49G GEN- 49G	Interleukin 8 receptor	1494 1442A>G	3
M98045	M98045	136510	4C3 GEN- 4C3	Homo sapiens folypolyglutamate synthetase mRNA, complete cds	802 732C>T	S
M98045	M98045	136510	4C3 GEN- 4C3	Homo sapiens folypolyglutamate synthetase mRNA, complete cds	1747 1677G>T	3
M98045	M98045	136510	4C3 GEN- 4C3	Homo sapiens folypolyglutamate synthetase mRNA, complete cds	1900 1830T>C	3
M98045	M98045	136510	4C3 GEN- 4C3	Homo sapiens folypolyglutamate synthetase mRNA, complete cds	1900 1830T>C	3
M98045	M98045	136510	4C3 GEN- 4C3	Homo sapiens folypolyglutamate synthetase mRNA, complete cds	1912 1842G>A	3
M98045	M98045	136510	4C3 GEN- 4C3	Homo sapiens folypolyglutamate synthetase mRNA, complete cds	1995 1925C>G	3
M98539	M98539	176803	GEN-SW	prostaglandin D2 synthase gene	157 158C>A	3
S63912	S63912	601233	GEN- 3EJ	D10S102=FBRNP [human, fetal brain, mRNA, 3043 nt]	2193 2163G>A	3
GABRB2	S77553	600232	GEN- 4FO	Gamma-aminobutyric acid (GABA) A receptor	438 438C>G	S
ADCYAP 1	S83513	102980	GEN- 3YA	pituitary adenylate cyclase activating polypeptide [human, mRNA, 1940 nt]	1521 1520G>A	3
U00672	U00672	146933	GEN-4A	Interleukin 10 receptor	3377 3316A>C	3
U00672	U00672	146933	GEN-4A	Interleukin 10 receptor	3524 3463A>G	3
GLP1R	U01157	138032	GEN-V3	Human glucagon-like	780 780C>A	F260L

GLP1R	U01157	138032	GEN-V3	peptide-1 receptor mRNA with CA dinucleotide repeat, complete cds Human glucagon-like peptide-1 receptor mRNA with CA dinucleotide repeat, complete cds	947 947G>C	G316A
GLP1R	U01157	138032	GEN-V3	Human glucagon-like peptide-1 receptor mRNA with CA dinucleotide repeat, complete cds	1200 1200C>A	S
U02326	U02326	142445	GEN-PE	Human clone ndf43 neu differentiation factor mRNA, complete cds	752 644G>A	G215E
SLO	U02632	600150	GEN-XA	Calcium-activated potassium channel mRNA, complete cds	2377 2377T>G	S793A
U02882	U02882	600129	GEN-XU	Human rolipram-sensitive 3,5-cyclic AMP phosphodiesterase mRNA, complete cds	1798 1690T>C	C564R
U02882	U02882	600129	GEN-XU	Human rolipram-sensitive 3,5-cyclic AMP phosphodiesterase mRNA, complete cds	1881 1773G>A	S
U02882	U02882	600129	GEN-XU	Human rolipram-sensitive 3,5-cyclic AMP phosphodiesterase mRNA, complete cds	4691 4583T>G	3
U04735	U04735	601100	GEN-15A	Human microsomal stress 70 protein ATPase core (stch) mRNA, complete cds	2120 2084A>G	3
NTRK3	U05012	191316	GEN-16V	Human receptor tyrosine kinase TrkC (NTRK3) mRNA, complete cds	364 209G>A	S70N
NTRK3	U05012	191316	GEN-16V	Human receptor tyrosine kinase TrkC (NTRK3) mRNA, complete cds	728 573C>T	S
NTRK3	U05012	191316	GEN-16V	Human receptor tyrosine kinase TrkC (NTRK3) mRNA, complete cds	1613 1458C>T	S
NTRK3	U05012	191316	GEN-16V	Human receptor tyrosine kinase TrkC (NTRK3) mRNA, complete cds	1643 1488G>C	S

DDH1	U05598	600450	GEN-184	16V	kinase TrkC (NTRK3) mRNA, complete cds Human dihydrodiol dehydrogenase mRNA, complete cds	38 15C>T	S
DDH1	U05598	600450	GEN-184		Human dihydrodiol dehydrogenase mRNA, complete cds	282 259A>T	S87C
DDH1	U05598	600450	GEN-184		Human dihydrodiol dehydrogenase mRNA, complete cds	350 327C>T	S
DDH1	U05598	600450	GEN-184		Human dihydrodiol dehydrogenase mRNA, complete cds	365 342T>C	S
DDH1	U05598	600450	GEN-184		Human dihydrodiol dehydrogenase mRNA, complete cds	464 441G>A	S
DDH1	U05598	600450	GEN-184		Human dihydrodiol dehydrogenase mRNA, complete cds	474 451A>G	M151V
DDH1	U05598	600450	GEN-184		Human dihydrodiol dehydrogenase mRNA, complete cds	532 509A>G	H170R
DDH1	U05598	600450	GEN-184		Human dihydrodiol dehydrogenase mRNA, complete cds	538 515T>A	L172Q
DDH1	U05598	600450	GEN-184		Human dihydrodiol dehydrogenase mRNA, complete cds	689 666T>C	S
DDH1	U05598	600450	GEN-184		Human dihydrodiol dehydrogenase mRNA, complete cds	806 783G>A	S
DDH1	U05598	600450	GEN-184		Human dihydrodiol dehydrogenase mRNA, complete cds	872 849G>T	S
DDH1	U05598	600450	GEN-184		Human dihydrodiol dehydrogenase mRNA, complete cds	952 929T>G	I310S
DDH1	U05598	600450	GEN-184		Human dihydrodiol dehydrogenase mRNA, complete cds	1020 997G>A	3

DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	1035 1012G>A	3
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	1112 1089C>T	3
U05875	U05875	147569	GEN-18J	Human clone pSK1 interferon gamma receptor accessory factor-1 (AF-1) mRNA, complete cds	2047 1399C>G	3
U05875	U05875	147569	GEN-18J	Human clone pSK1 interferon gamma receptor accessory factor-1 (AF-1) mRNA, complete cds	2087 1439T>C	3
U07225	U07225	600041	GEN-1DM	P2Y2 purinoceptor	2008 1763G>A	3
U07364	U07364	600504	GEN-1DS	Inwardly rectifying potassium channel	982 885G>A	S
U07364	U07364	600504	GEN-1DS	Inwardly rectifying potassium channel	1099 1002A>G	S
U07364	U07364	600504	GEN-1DS	Inwardly rectifying potassium channel	1537 1440G>A	3
U07364	U07364	600504	GEN-1DS	Inwardly rectifying potassium channel	1714 1617G>A	3
AMPH	U07616	600418	GEN-1ED	potassium channel	1856 1746G>T	S
AMPH	U07616	600418	GEN-1ED	Human amphiphysin mRNA, complete cds	1901 1791G>A	S
AMPH	U07616	600418	GEN-1ED	Human amphiphysin mRNA, complete cds	2289 2179A>G	3
U08989	U08989	133550	GEN-CBZ	Human glutamate transporter mRNA, complete cds	684 519C>T	S
U08989	U08989	133550	GEN-CBZ	Human glutamate transporter mRNA, complete cds	1617 1452T>C	S
U09002	U09002	138253	GEN-1G8	Glutamate Aspartate receptor NMDA 2A	1430 1275A>G	S
U09002	U09002	138253	GEN-1G8	Glutamate Aspartate receptor NMDA 2A	4468 4313T>C	M1438T
U09002	U09002	138253	GEN-1G8	Glutamate Aspartate receptor NMDA 2A	4671 4516G>T	3

U09002	U09002	138253	1G8 GEN-	receptor NMDA 2A	5562 5407delC	F
U09002	U09002	138253	1G8 GEN-	Glutamate Aspartate receptor NMDA 2A	5765 5610C>T	3
SLC18A3	U09210	600336	1G8 GEN-	Glutamate Aspartate receptor NMDA 2A	1369 927A>G	S
SLC18A3	U09210	600336	4F3	Human vesicular acetylcholine transporter mRNA, complete cds	1567 1125C>G	S
SLC18A3	U09210	600336	4F3	Human vesicular acetylcholine transporter mRNA, complete cds	2080 1638G>T	3
SLC18A3	U09210	600336	4F3	Human vesicular acetylcholine transporter mRNA, complete cds	2199 1757G>A	3
SLC18A3	U09210	600336	4F3	Human vesicular acetylcholine transporter mRNA, complete cds	2349 1907G>T	3
U09806	U09806	None	GEN- 4FZ	Human vesicular acetylcholine transporter mRNA, complete cds	120 120T>C	S
U09806	U09806	None	GEN- 4FZ	Human methylenetetrahydrofolate reductase mRNA, partial cds	473 473G>A	R158Q
U09806	U09806	None	GEN- 4FZ	Human methylenetetrahydrofolate reductase mRNA, partial cds	550 550C>T	F
U09806	U09806	None	GEN- 4FZ	Human methylenetetrahydrofolate reductase mRNA, partial cds	668 668C>T	A223V
U09806	U09806	None	GEN- 4FZ	Human methylenetetrahydrofolate reductase mRNA, partial cds	1059 1059T>C	S
U09806	U09806	None	GEN-	Human methylenetetrahydrofolate reductase mRNA, partial cds	1289 1289C>A	E430A

U09806	U09806	None	GEN-4FZ	4FZ	methylenetetrahydrofolate reductase mRNA, partial cds	1308 1308T>C	3
OPRD1	U10504	165195	GEN-4F5	4F5	Human delta opiate receptor mRNA, complete cds	921 921T>C	S
U12507	U12507	600681	GEN-1MD	1MD	Cardiac inward rectifier potassium channel (HH-IRK1)	338 13C>A	S
U12507	U12507	600681	GEN-1MD	1MD	Cardiac inward rectifier potassium channel (HH-IRK1)	1597 1272G>A	S
U12779	U12779	None	GEN-1MV	1MV	Human MAP kinase activated protein kinase 2 mRNA, complete cds	450 72C>G	S
U12779	U12779	None	GEN-1MV	1MV	Human MAP kinase activated protein kinase 2 mRNA, complete cds	1329 951C>T	S
U13737	U13737	600636	GEN-1PC	1PC	Human cysteine protease CPP32 isoform alpha mRNA, complete cds	2356 2132A>C	3
U13737	U13737	600636	GEN-1PC	1PC	Human cysteine protease CPP32 isoform alpha mRNA, complete cds	2535 2311C>T	3
U16125	U16125	138245	GEN-1XK	1XK	Human cysteine protease CPP32 isoform alpha mRNA, complete cds	2563 2563T>G	C855G
U16957	U16957	300034	GEN-1L	GEN-1L	Angiotensin receptor AT2	263 123T>C	S
U16957	U16957	300034	GEN-1L	GEN-1L	Angiotensin receptor AT2	883 743G>A	R248K
NOS1	U17327	163731	GEN-209	GEN-209	Human neuronal nitric oxide synthase (NOS1) mRNA, complete cds	3391 2706C>T	S
PDE4A	U18087	600126	GEN-214	GEN-214	Human 3,5-cyclic AMP phosphodiesterase HPDE4A6 mRNA, complete cds	642 633T>G	S
PDE4A	U18087	600126	GEN-214	GEN-214	Human 3,5-cyclic AMP phosphodiesterase	804 795T>C	S

PDE4A	U18087	600126	GEN-214	HPDE4A6 mRNA, complete cds	1616	1607A>C	E536A
				Human 3,5-cyclic AMP phosphodiesterase HPDE4A6 mRNA, complete cds			
U19251	U19251	600355	GEN-221	Homo sapiens neuronal apoptosis inhibitory protein mRNA, complete cds	2223	1932T>G	F644L
U19251	U19251	600355	GEN-221	Homo sapiens neuronal apoptosis inhibitory protein mRNA, complete cds	3046	2755C>T	P919S
U19251	U19251	600355	GEN-221	Homo sapiens neuronal apoptosis inhibitory protein mRNA, complete cds	5503	5212A>G	3
U19251	U19251	600355	GEN-221	Homo sapiens neuronal apoptosis inhibitory protein mRNA, complete cds	5634	5343A>G	3
U19251	U19251	600355	GEN-221	Homo sapiens neuronal apoptosis inhibitory protein mRNA, complete cds	5644	5353A>G	3
U19487	U19487	176804	GEN-41	PROSTAGLANDIN E2 RECEPTOR, EP2 SUBTYPE	231	75A>T	S
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	53	(-43)T>C	5
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	175	80G>A	R27H
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	175	80G>A	R27H
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	341	246C>G	S
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	791	696C>T	S
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	1067	972G>A	S
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	2100	2005*2006ins G	F
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	2582	2487T>G	3
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	2582	2487T>G	3

U19720	U19720	600424	GEN-11	(SLC19A1) Folate Transporter	2617 2522C>T	3
U19720	U19720	600424	GEN-11	(SLC19A1) Folate Transporter	2617 2522C>T	3
U19720	U19720	600424	GEN-11	(SLC19A1) Folate Transporter	2552 2557T>C	3
U20157	U20157	601690	GEN-234	Human platelet-activating factor acetylhydrolase mRNA, complete cds	1297 1136T>C	V379A
U23143	U23143	138450	GEN- MIY	Human mitochondrial serine hydroxymethyltransferase gene, nuclear encoded mitochondrion protein, complete cds	506 506T>G	F169C
U25029	U25029	138040	GEN-82	Glucocorticoid receptor alpha	335 335C>T	3
U25029	U25029	138040	GEN-82	Glucocorticoid receptor alpha	386 386T>C	3
U25029	U25029	138040	GEN-82	Glucocorticoid receptor alpha	1069 1069C>T	3
U26553	U26553	114131	GEN-66	Calcitonin Receptor	1412 1340C>T	P447L
U26553	U26553	114131	GEN-66	Calcitonin Receptor	1515 1443T>C	3
U26648	U26648	603189	GEN-IC	Syntaxin 5A	501 475C>T	R159W
U26648	U26648	603189	GEN-IC	Syntaxin 5A	1270 1244G>A	3
U26648	U26648	603189	GEN-IC	Syntaxin 5A	1288 1262G>T	3
U27699	U27699	603080	GEN- 2C9	Human pephBGT-1 betaine-GABA transporter mRNA, complete cds	2841 2255C>T	3
U32315	U32315	600876	GEN-IL	syntaxin 3	411 373C>T	R125W
U32315	U32315	600876	GEN-IL	syntaxin 3	1601 1563G>A	3
U32500	U32500	162642	GEN-1P	Neuropeptide Y2	407 159C>T	S
U32500	U32500	162642	GEN-1P	Neuropeptide Y2	833 585T>C	S
U32500	U32500	162642	GEN-1P	Neuropeptide Y2	833 585T>C	S
U32500	U32500	162642	GEN-1P	Neuropeptide Y2	1184 936T>C	S
U32500	U32500	162642	GEN-1P	Neuropeptide Y2	1184 936T>C	S
U32500	U32500	162642	GEN-1P	Neuropeptide Y2	1706 1458- 1460TAT>TA	3

U32500	U32500	162642	GEN-1P	Neuropeptide Y2	1706 1458- 1460delTAT	T	3
U32500	U32500	162642	GEN-1P	Neuropeptide Y2	2782 2534*2535ins CA	F	F
U32989	U32989	191070	GEN- 2JH	Human tryptophan oxygenase (TDO) mRNA, complete cds	991 927G>A	S	S
U33052	U33052	602549	GEN-2JL	Human lipid-activated, protein kinase PRK2 mRNA, complete cds	34 25G>C	E9Q	E9Q
U33052	U33052	602549	GEN-2JL	Human lipid-activated, protein kinase PRK2 mRNA, complete cds	430 421T>C	S	S
U33052	U33052	602549	GEN-2JL	Human lipid-activated, protein kinase PRK2 mRNA, complete cds	1112 1103T>G	F368C	F368C
U33053	U33053	601032	GEN- 2JK	Human lipid-activated protein kinase PRK1 mRNA, complete cds	656 572A>G	D191G	D191G
U33053	U33053	601032	GEN- 2JK	Human lipid-activated protein kinase PRK1 mRNA, complete cds	2608 2524G>A	A842T	A842T
U33053	U33053	601032	GEN- 2JK	Human lipid-activated protein kinase PRK1 mRNA, complete cds	2649 2565G>A	S	S
U33053	U33053	601032	GEN- 2JK	Human lipid-activated protein kinase PRK1 mRNA, complete cds	2713 2629C>T	S	S
U33053	U33053	601032	GEN- 2JK	Human lipid-activated protein kinase PRK1 mRNA, complete cds	2785 2701G>A	V901I	V901I
U33053	U33053	601032	GEN- 2JK	Human lipid-activated protein kinase PRK1 mRNA, complete cds	2846 2762C>G	A921G	A921G
U33053	U33053	601032	GEN- 2JK	Human lipid-activated protein kinase PRK1 mRNA, complete cds	2856 2772C>T	S	S
U33053	U33053	601032	GEN- 2JK	Human lipid-activated protein kinase PRK1 mRNA, complete cds	2860 2776G>A	A926T	A926T

U33053	U33053	601032	GEN-2JK	Human lipid-activated protein kinase PRK1 mRNA, complete cds	2889 2805C>T	S
U33053	U33053	601032	GEN-2JK	Human lipid-activated protein kinase PRK1 mRNA, complete cds	2895 2811C>T	S
U33053	U33053	601032	GEN-2JK	Human lipid-activated protein kinase PRK1 mRNA, complete cds	2954 2870C>T	3
U33632	U33632	601745	GEN-IN	Two P-domain K ⁺ channel TWIK-1 mRNA	1386 1204G>A	3
PSEN2	U34349	600759	GEN-2L2	Human seven transmembrane domain protein (AD3LP/AD5) mRNA, complete cds	160 69C>T	S
PSEN2	U34349	600759	GEN-2L2	Human seven transmembrane domain protein (AD3LP/AD5) mRNA, complete cds	220 129C>T	S
PSEN2	U34349	600759	GEN-2L2	Human seven transmembrane domain protein (AD3LP/AD5) mRNA, complete cds	220 129C>T	S
PSEN2	U34349	600759	GEN-2L2	Human seven transmembrane domain protein (AD3LP/AD5) mRNA, complete cds	352 261C>T	S
PSEN2	U34349	600759	GEN-2L2	Human seven transmembrane domain protein (AD3LP/AD5) mRNA, complete cds	352 261C>T	S
PSEN2	U34349	600759	GEN-2L2	Human seven transmembrane domain protein (AD3LP/AD5) mRNA, complete cds	1437 1346C>T	3
PSEN2	U34349	600759	GEN-2L2	Human seven transmembrane domain protein (AD3LP/AD5) mRNA, complete cds	1654 1563C>G	3
PPP2R4	U37352	601645	GEN-2O5	Human protein phosphatase 2A Balphat1	2084 1996G>A	3

TAC2	U37529	162320	GEN-2OH	regulatory subunit mRNA, complete cds	644 499G>A	3
TAC2	U37529	162320	GEN-2OH	Substance P beta-PPT-A	694 549T>C	3
TAC2	U37529	162320	GEN-2OH	Substance P beta-PPT-A	799 654A>G	3
TAC2	U37529	162320	GEN-2OH	Substance P beta-PPT-A	826 681C>T	3
U39412	U39412	None	GEN-2Q5	Homo sapiens alpha SNAP mRNA, complete cds	138 71C>T	S24L
U39412	U39412	None	GEN-2Q5	Homo sapiens alpha SNAP mRNA, complete cds	290 223C>T	L75F
U39412	U39412	None	GEN-2Q5	Homo sapiens alpha SNAP mRNA, complete cds	473 406G>A	V136M
U39412	U39412	None	GEN-2Q5	Homo sapiens alpha SNAP mRNA, complete cds	651 584C>G	T195S
U40347	U40347	600950	GEN-2RK	Human serotonin N-acetyltransferase mRNA, complete cds	382 148G>A	E50K
U40396	U40396	602691	GEN-6W	Steroid receptor coactivator (SRC-1)	285 229A>C	K77Q
U40396	U40396	602691	GEN-6W	Steroid receptor coactivator (SRC-1)	314 258A>T	K86N
U40396	U40396	602691	GEN-6W	Steroid receptor coactivator (SRC-1)	336 280C>T	P94S
U40396	U40396	602691	GEN-6W	Steroid receptor coactivator (SRC-1)	688 632C>T	T211I
U40396	U40396	602691	GEN-6W	Steroid receptor coactivator (SRC-1)	970 914C>A	A305E
U40396	U40396	602691	GEN-6W	Steroid receptor coactivator (SRC-1)	1511 1455G>A	S
U40396	U40396	602691	GEN-6W	Steroid receptor coactivator (SRC-1)	2377 2321C>T	T774M
U40396	U40396	602691	GEN-6W	Steroid receptor coactivator (SRC-1)	2730 2674C>T	P892S
U40583	U40583	118511	GEN-4O	Nicotinic, Cholinergic receptor alpha 7	661 654T>C	S
U40583	U40583	118511	GEN-4O	Nicotinic, Cholinergic receptor alpha 7	697 690A>G	S

U40583	U40583	118511	GEN-4O	Nicotinic, Cholinergic receptor alpha 7	940 933G>A	S
U40583	U40583	118511	GEN-4O	Nicotinic, Cholinergic receptor alpha 7	1276 1269T>C	S
U40583	U40583	118511	GEN-4O	Nicotinic, Cholinergic receptor alpha 7	1790 1783A>T	3
U40583	U40583	118511	GEN-4O	Nicotinic, Cholinergic receptor alpha 7	1792 1785T>A	3
U43030	U43030	600435	GEN-LFI	Human cardiotrophin-1 (CTF1) mRNA, complete cds	1404 1372C>T	3
LEPR	U43168	601007	GEN- 2UN	Human leptin receptor (Ob- r) mRNA, complete cds	446 253A>G	T85A
LEPR	U43168	601007	GEN- 2UN	Human leptin receptor (Ob- r) mRNA, complete cds	519 326A>G	K109R
LEPR	U43168	601007	GEN- 2UN	Human leptin receptor (Ob- r) mRNA, complete cds	1222 1029T>C	S
LEPR	U43168	601007	GEN- 2UN	Human leptin receptor (Ob- r) mRNA, complete cds	2161 1968G>C	K656N
LEPR	U43168	601007	GEN- 2UN	Human leptin receptor (Ob- r) mRNA, complete cds	2174 1981A>C	T661P
LEPR	U43168	601007	GEN- 2UN	Human leptin receptor (Ob- r) mRNA, complete cds	3151 2958C>T	S
LEPR	U43168	601007	GEN- 2UN	Human leptin receptor (Ob- r) mRNA, complete cds	3250 3057G>A	S
U45448	U45448	600845	GEN-4FI	Human P2x1 receptor mRNA, complete cds	1424 1228A>G	3
U45448	U45448	600845	GEN-4FI	Human P2x1 receptor mRNA, complete cds	1604 1408C>G	3
U45448	U45448	600845	GEN-4FI	Human P2x1 receptor mRNA, complete cds	1719 1523G>A	3
U45448	U45448	600845	GEN-4FI	Human P2x1 receptor mRNA, complete cds	1827 1631G>A	3
U45448	U45448	600845	GEN-4FI	Human P2x1 receptor mRNA, complete cds	2286 2090G>A	3
U47741	U47741	600140	GEN-6X	CREB-binding protein (CBP)	5369 5171A>T	E1724V
U47741	U47741	600140	GEN-6X	CREB-binding protein (CBP)	5372 5174A>T	D1725V
U49516	U49516	312861	GEN-1Q	Serotonin 5-HT receptors 5-HT2C	2915 2187A>C	3

U49516	U49516	312861	GEN-1Q	Serotonin 5-HT receptors 5-HT2C	2947 2219A>G	3
U55206	U55206	None	GEN-35Z	Homo sapiens human gamma-glutamyl hydrolase (hGH) mRNA, complete cds	75 16T>C	C6R
U55206	U55206	None	GEN-35Z	Homo sapiens human gamma-glutamyl hydrolase (hGH) mRNA, complete cds	150 91G>A	A31T
U55206	U55206	None	GEN-35Z	Homo sapiens human gamma-glutamyl hydrolase (hGH) mRNA, complete cds	511 452C>T	T151I
U55206	U55206	None	GEN-35Z	Homo sapiens human gamma-glutamyl hydrolase (hGH) mRNA, complete cds	1161 1102A>G	3
U56976	U56976	171891	GEN-379	Human calmodulin dependent phosphodiesterase PDE1B1 mRNA, complete cds	1510 1476C>T	S
U57317	U57317	None	GEN-6Y	p300/CBP-associated factor (P/CAF)	2764 2306A>G	D769G
CHRNA2	U62431	118502	GEN-4EN	Nicotinic, Cholinergic receptor alpha 2	2296 1742C>G	3
CHRNA2	U62431	118502	GEN-4EN	Nicotinic, Cholinergic receptor alpha 2	2387 1833C>T	3
CHRNA2	U62431	118502	GEN-4EN	Nicotinic, Cholinergic receptor alpha 2	2504 1950G>T	3
CHRNA2	U62431	118502	GEN-4EN	Nicotinic, Cholinergic receptor alpha 2	2538 1984G>A	3
U62433	U62433	118504	GEN-4P	Nicotinic, Cholinergic receptor alpha 4	870 639C>T	S
U62433	U62433	118504	GEN-4P	Nicotinic, Cholinergic receptor alpha 4	870 639C>T	S
U62433	U62433	118504	GEN-4P	Nicotinic, Cholinergic receptor alpha 4	909 678C>T	S
U62433	U62433	118504	GEN-4P	Nicotinic, Cholinergic receptor alpha 4	909 678C>T	S

U62433	U62433	118504	GEN-4P	Nicotinic, Cholinergic receptor alpha 4	1440 1209T>G	S
U62433	U62433	118504	GEN-4P	Nicotinic, Cholinergic receptor alpha 4	1458 1227C>T	S
U62433	U62433	118504	GEN-4P	Nicotinic, Cholinergic receptor alpha 4	1860 1629C>T	S
U62433	U62433	118504	GEN-4P	Nicotinic, Cholinergic receptor alpha 4	1890 1659G>A	S
U62768	U62768	151300	GEN-3CR	Human oxytocinase splice variant 1 mRNA, complete cds	3356 3295G>C	3
U62768	U62768	151300	GEN-3CR	Human oxytocinase splice variant 1 mRNA, complete cds	3547 3486C>T	3
U71321	U71321	602623	GEN-2TW	Human FK506-binding protein FKBP51 mRNA, complete cds	1248 1095C>T	S
U71321	U71321	602623	GEN-2TW	Human FK506-binding protein FKBP51 mRNA, complete cds	1425 1272G>A	S
U72661	U72661	602062	GEN-3LK	Human ninjurin1 mRNA, complete cds	1205 1185C>A	3
U75283	U75283	None	GEN-3NV	Human sigma receptor mRNA, complete cds	251 204G>A	S
U75283	U75283	None	GEN-3NV	Human sigma receptor mRNA, complete cds	1625 1578A>C	3
U81375	U81375	602193	GEN-3VO	Human placental equilibrative nucleoside transporter 1 (hENT1) mRNA, complete cds	1989 1811G>A	3
U81375	U81375	602193	GEN-3VO	Human placental equilibrative nucleoside transporter 1 (hENT1) mRNA, complete cds	1996 1818C>T	3
U81375	U81375	602193	GEN-3VO	Human placental equilibrative nucleoside transporter 1 (hENT1) mRNA, complete cds	2045 1867T>C	3
U81504	U81504	603401	GEN-3VX	Homo sapiens beta-3A-adaptin subunit of the AP-3 complex mRNA, complete	1775 1683C>T	S

U81504	U81504	603401	GEN-3VX	Homo sapiens beta-3A-adaptin subunit of the AP-3 complex mRNA, complete cds	2108 2016T>C	S
U81504	U81504	603401	GEN-3VX	Homo sapiens beta-3A-adaptin subunit of the AP-3 complex mRNA, complete cds	2668 2576G>T	S859I
U81554	U81554	602122	GEN-3VW	Homo sapiens CaM kinase II isoform mRNA, complete cds	939 727A>G	3
U84404	U84404	601623	GEN-83	Ubiquitin protein ligase E3A	1003 417A>T	S
U84404	U84404	601623	GEN-83	Ubiquitin protein ligase E3A	1386 800T>G	V267G
U84404	U84404	601623	GEN-83	Ubiquitin protein ligase E3A	1930 1344A>G	S
U84404	U84404	601623	GEN-83	Ubiquitin protein ligase E3A	2299 1713A>G	S
U95025	U95025	601116	GEN-4FX	Homo sapiens metabotropic glutamate receptor 8 (GRM8) mRNA, complete cds	744 744T>C	S
U97669	U97669	600276	GEN-4BU	Homo sapiens Notch3 (NOTCH3) mRNA, complete cds	7712 7634T>G	3
U97669	U97669	600276	GEN-4BU	Homo sapiens Notch3 (NOTCH3) mRNA, complete cds	7852 7774A>G	3
U97669	U97669	600276	GEN-4BU	Homo sapiens Notch3 (NOTCH3) mRNA, complete cds	7881 7803G>A	3
U97669	U97669	600276	GEN-4BU	Homo sapiens Notch3 (NOTCH3) mRNA, complete cds	7934 7856T>C	3
V00518	V00518	118850	GEN-P4	Human messenger RNA for chorionic gonadotropin	565 515T>C	3
V00519	V00519	139250	GEN-4U	Growth hormone 1	299 259C>A	P87T
V00519	V00519	139250	GEN-4U	Growth hormone 1	524 484G>T	G162W
IFNB1	V00546	147640	GEN-TV	Messenger RNA for human	474 410T>G	L137R

V00548	V00548	147562	GEN-P2	fibroblast interferon	119	119G>A	R40K
				Human messenger RNA for leukocyte (alpha-2) interferon			
V00566	V00566	176760	GEN-4V	Prolactin	574	570G>A	S
V00571	V00571	122560	GEN-CBO	corticotropin releasing factor	822	637delA	F
V00571	V00571	122560	GEN-CBO	corticotropin releasing factor	837	652G>A	3
X00734	X00734	None	GEN-MST	Human beta-tubulin gene (5-beta) with ten Alu family members	1059	1059G>T	S
X01394	X01394	191160	GEN-4Y	Tumor necrosis factor	125	(-28)C>T	5
X02317	X02317	147450	GEN-KM	Superoxide dismutase 1 (Cu/Zn)	614	550A>C	3
X02415	X02415	134850	GEN-MJO	Human gene for fibrinogen gamma chain	1000	949G>A	D317N
X02812	X02812	190180	GEN-XR	Human mRNA for transforming growth factor-beta (TGF-beta)	870	29C>T	P10L
X02812	X02812	190180	GEN-XR	Human mRNA for transforming growth factor-beta (TGF-beta)	979	138C>G	I46M
X02812	X02812	190180	GEN-XR	Human mRNA for transforming growth factor-beta (TGF-beta)	1632	791C>T	T264I
X02812	X02812	190180	GEN-XR	Human mRNA for transforming growth factor-beta (TGF-beta)	1807	966C>T	S
X02812	X02812	190180	GEN-XR	Human mRNA for transforming growth factor-beta (TGF-beta)	1930	1089G>A	S
X02812	X02812	190180	GEN-XR	Human mRNA for transforming growth factor-beta (TGF-beta)	1942	1101C>T	S
X02812	X02812	190180	GEN-XR	Human mRNA for transforming growth factor-beta (TGF-beta)	2013	1172G>A	S391N
X03172	X03172	192340	GEN-ZM	Human mRNA for vasopressin precursor	379	356T>G	V119G
X03635	X03635	133430	GEN-50	estrogen receptors	390	30T>C	S

X03635	X03635	133430	GEN-50	estrogen receptors	390 30T>C	S
X03635	X03635	133430	GEN-50	estrogen receptors	424 64G>C	E22Q
X03635	X03635	133430	GEN-50	estrogen receptors	617 257C>T	A86V
X03635	X03635	133430	GEN-50	estrogen receptors	621 261G>C	S
X03635	X03635	133430	GEN-50	estrogen receptors	829 469C>T	F
X03635	X03635	133430	GEN-50	estrogen receptors	1335 975C>G	S
X03635	X03635	133430	GEN-50	estrogen receptors	1335 975C>G	S
X03635	X03635	133430	GEN-50	estrogen receptors	1451 1091T>A	V364E
X03635	X03635	133430	GEN-50	estrogen receptors	1674 1314G>A	M438I
X03635	X03635	133430	GEN-50	estrogen receptors	2142 1782A>G	S
X03635	X03635	133430	GEN-50	estrogen receptors	2354 1994A>G	3
X03635	X03635	133430	GEN-50	estrogen receptors	2550 2190A>C	3
X03635	X03635	133430	GEN-50	estrogen receptors	2733 2373C>G	3
X03635	X03635	133430	GEN-50	estrogen receptors	3181 2821T>C	3
X03635	X03635	133430	GEN-50	estrogen receptors	3338 2978C>T	3
X03635	X03635	133430	GEN-50	estrogen receptors	3652 3292- 3294CCT>CC	3
X03635	X03635	133430	GEN-50	estrogen receptors	3652 3292- 3294delCCT	3
X03635	X03635	133430	GEN-50	estrogen receptors	3896 3536C>A	3
X03635	X03635	133430	GEN-50	estrogen receptors	4378 4018T>C	3
X03635	X03635	133430	GEN-50	estrogen receptors	6287 5927T>C	3
X04741	X04741	191342	GEN-KU	UBIQUITIN CARBOXYL- TERMINAL HYDROLASE	51 20C>A	S7Y
X04741	X04741	191342	GEN-KU	UBIQUITIN CARBOXYL- TERMINAL HYDROLASE	291 260C>G	A87G
X04741	X04741	191342	GEN-KU	UBIQUITIN CARBOXYL- TERMINAL HYDROLASE	296 265G>C	A89P
CST3	X05607	105150	GEN-189	Human mRNA for cysteine proteinase inhibitor	62 (-13)C>G	5
CST3	X05607	105150	GEN-189	Human mRNA for cysteine proteinase inhibitor	455 381C>T	S

CST3	X05607	105150	GEN-189	Human mRNA for cysteine proteinase inhibitor	550 476C>T	3
CST3	X05607	105150	GEN-189	precursor cystatin C	632 558A>C	3
CST3	X05607	105150	GEN-189	Human mRNA for cysteine proteinase inhibitor	647 573G>A	3
CST3	X05607	105150	GEN-189	precursor cystatin C	713 639C>T	3
CST3	X05607	105150	GEN-189	Human mRNA for cysteine proteinase inhibitor	746 672A>C	3
X06318	X06318	176970	GEN-KY	precursor cystatin C	83 (-54)G>C	5
X06318	X06318	176970	GEN-KY	Protein kinase C, beta 1	940 804G>A	S
X06318	X06318	176970	GEN-KY	Protein kinase C, beta 1	1327 1191T>C	S
X06318	X06318	176970	GEN-KY	Protein kinase C, beta 1	1906 1770C>T	S
X06562	X06562	600946	GEN-6D	Growth hormone receptor	3392 3349A>T	3
X06562	X06562	600946	GEN-6D	Growth hormone receptor	4145 4102G>A	3
X07674	X07674	138130	GEN-1EC	Human mRNA for glutamate dehydrogenase (EC 1.4.1.3., GDH)	266 253C>T	S
X07674	X07674	138130	GEN-1EC	Human mRNA for glutamate dehydrogenase (EC 1.4.1.3., GDH)	272 259G>A	E87K
X07674	X07674	138130	GEN-1EC	Human mRNA for glutamate dehydrogenase (EC 1.4.1.3., GDH)	288 275G>A	R92Q
X07674	X07674	138130	GEN-1EC	Human mRNA for glutamate dehydrogenase (EC 1.4.1.3., GDH)	292 279G>A	S
X07674	X07674	138130	GEN-1EC	Human mRNA for glutamate dehydrogenase (EC 1.4.1.3., GDH)	595 582T>C	S
X07674	X07674	138130	GEN-1EC	Human mRNA for glutamate dehydrogenase (EC 1.4.1.3., GDH)	598 585T>A	D195E
X07674	X07674	138130	GEN-1EC	Human mRNA for glutamate dehydrogenase (EC 1.4.1.3., GDH)	646 633A>G	S

1EC	glutamate dehydrogenase (EC 1.4.1.3., GDH)	GEN-1EC	X07674	138130	X07674	138130	668	655A>G	I219V
1EC	glutamate dehydrogenase (EC 1.4.1.3., GDH)	GEN-1EC	X07674	138130	X07674	138130	693	680G>A	S227N
1EC	glutamate dehydrogenase (EC 1.4.1.3., GDH)	GEN-1EC	X07674	138130	X07674	138130	721	708C>T	S
1EC	glutamate dehydrogenase (EC 1.4.1.3., GDH)	GEN-1EC	X07674	138130	X07674	138130	859	846T>C	S
1EC	glutamate dehydrogenase (EC 1.4.1.3., GDH)	GEN-1EC	X07674	138130	X07674	138130	1134	1121C>T	A374V
1EC	glutamate dehydrogenase (EC 1.4.1.3., GDH)	GEN-1EC	X07674	138130	X07674	138130	1164	1151G>C	S384T
1EC	glutamate dehydrogenase (EC 1.4.1.3., GDH)	GEN-1EC	X07674	138130	X07674	138130	1255	1242C>T	S
1EC	glutamate dehydrogenase (EC 1.4.1.3., GDH)	GEN-1EC	X07674	138130	X07674	138130	1415	1402A>C	M468L
1EC	glutamate dehydrogenase (EC 1.4.1.3., GDH)	GEN-1EC	X07674	138130	X07674	138130	1427	1414G>T	F
1EC	glutamate dehydrogenase (EC 1.4.1.3., GDH)	GEN-1EC	X07674	138130	X07674	138130	1501	1488G>T	R496S
1EC	glutamate dehydrogenase (EC 1.4.1.3., GDH)	GEN-1EC	X07674	138130	X07674	138130	1528	1515C>T	S
1EC	glutamate dehydrogenase (EC 1.4.1.3., GDH)	GEN-1EC	X07674	138130	X07674	138130	1539	1526G>C	G509A
1EC	glutamate dehydrogenase (EC 1.4.1.3., GDH)	GEN-1EC	X07674	138130	X07674	138130	1581	1568G>A	R523H

X07674	X07674	138130	GEN-1EC	Human mRNA for glutamate dehydrogenase (EC 1.4.1.3., GDH)	1633 1620T>C	S
X07674	X07674	138130	GEN-1EC	Human mRNA for glutamate dehydrogenase (EC 1.4.1.3., GDH)	1645 1632G>A	S
X07674	X07674	138130	GEN-1EC	Human mRNA for glutamate dehydrogenase (EC 1.4.1.3., GDH)	1665 1652A>G	N551S
X07674	X07674	138130	GEN-1EC	Human mRNA for glutamate dehydrogenase (EC 1.4.1.3., GDH)	1717 1704T>A	3
X07674	X07674	138130	GEN-1EC	Human mRNA for glutamate dehydrogenase (EC 1.4.1.3., GDH)	1830 1817G>A	3
SOD2	X07834	147460	GEN-1ES	Human mRNA for manganese superoxide dismutase (EC 1.15.1.1)	44 40C>G	P14A
SOD2	X07834	147460	GEN-1ES	Human mRNA for manganese superoxide dismutase (EC 1.15.1.1)	51 47T>C	V16A
SOD2	X07834	147460	GEN-1ES	Human mRNA for manganese superoxide dismutase (EC 1.15.1.1)	198 194C>A	T65N
SOD2	X07834	147460	GEN-1ES	Human mRNA for manganese superoxide dismutase (EC 1.15.1.1)	249 245T>C	I82T
X12953	X12953	179509	GEN-1NA	Human mRNA for related and member of ras family	723 515A>C	Q172P
X13561	X13561	147910	GEN-1OH	Human mRNA for preprokallikrein (EC 3.4.21)	54 18G>T	S
X13561	X13561	147910	GEN-1OH	Human mRNA for preprokallikrein (EC 3.4.21)	441 405T>C	S
X13561	X13561	147910	GEN-1OH	Human mRNA for preprokallikrein (EC 3.4.21)	469 433G>C	E145Q
X13561	X13561	147910	GEN-1OH	Human mRNA for preprokallikrein (EC 3.4.21)	592 556A>G	K186E
X13589	X13589	107910	GEN-56	Cytochrome P450, subfamily XIX (aromatization of	364 240A>G	S

X13589	X13589	107910	GEN-56	androgens) Cytochrome P450, subfamily XIX (aromatization of androgens)	914 790C>T	R264C
X13589	X13589	107910	GEN-56	Cytochrome P450, subfamily XIX (aromatization of androgens)	914 790C>T	R264C
X13589	X13589	107910	GEN-56	androgens) Cytochrome P450, subfamily XIX (aromatization of androgens)	1655 1531C>T	3
X13589	X13589	107910	GEN-56	androgens) Cytochrome P450, subfamily XIX (aromatization of androgens)	1796 1672G>T	3
X13629	X13629	107690	GEN-100	Human intestinal mRNA for apolipoprotein A-IV	881 836G>A	R279K
X13629	X13629	107690	GEN-100	Human intestinal mRNA for apolipoprotein A-IV	1185 1140G>T	Q380H
X13629	X13629	107690	GEN-100	Human intestinal mRNA for apolipoprotein A-IV	1302 1257^1258ins CTGT	F
X13916	X13916	107770	GEN-1Q1	Human mRNA for LDL- receptor related protein	2805 2339C>T	T780I
X13916	X13916	107770	GEN-1Q1	Human mRNA for LDL- receptor related protein	8608 8142G>A	S
X13916	X13916	107770	GEN-1Q1	Human mRNA for LDL- receptor related protein	8923 8457C>T	S
X13916	X13916	107770	GEN-1Q1	Human mRNA for LDL- receptor related protein	9034 8568G>T	S
X13916	X13916	107770	GEN-1Q1	Human mRNA for LDL- receptor related protein	9040 8574C>T	S
X13916	X13916	107770	GEN-1Q1	Human mRNA for LDL- receptor related protein	9391 8925T>C	S
LIF	X13967	159540	GEN-1PZ	Human mRNA for leukaemia inhibitory factor (LIF/HILDA)	3710 3666T>G	3
CLU	X14723	185430	GEN-1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1	131 84C>T	S

CLU	X14723	185430	GEN-1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	429 382G>T	V128F
CLU	X14723	185430	GEN-1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	836 789C>T	S
CLU	X14723	185430	GEN-1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	1234 1187C>T	S396L
CLU	X14723	185430	GEN-1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	1372 1325A>T	Y442F
CLU	X14723	185430	GEN-1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	1482 1435C>T	3
CLU	X14723	185430	GEN-1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	1548 1501C>T	3
CLU	X14723	185430	GEN-1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	1645 1598A>T	3
X14766	X14766	137160	GEN-1X	Gamma-aminobutyric acid (GABA) A receptor	370 156C>T	S
CHRN1	X14830	100710	GEN-4EK	Nicotinic, Cholinergic receptor beta 1	1375 1359C>T	S
CHRN1	X14830	100710	GEN-4EK	Nicotinic, Cholinergic receptor beta 1	1591 1575T>C	3
X15263	X15263	None	GEN-4EK	Muscarinic receptor, CHRM1	1144 1044G>A	S
X15357	X15357	108960	GEN-KUV	Human mRNA for natriuretic peptide receptor (ANP-A receptor)	1066 1023G>C	M341I
X15357	X15357	108960	GEN-	Human mRNA for	1657 1614C>T	S

X15357	X15357	108960	KUV	natriuretic peptide receptor (ANP-A receptor)	2859 2816G>A	R939Q
X15357	X15357	108960	GEN-KUV	Human mRNA for natriuretic peptide receptor (ANP-A receptor)	2983 2940G>A	S
X15357	X15357	108960	GEN-KUV	Human mRNA for natriuretic peptide receptor (ANP-A receptor)	3259 3216delC	F
X15357	X15357	108960	GEN-KUV	Human mRNA for natriuretic peptide receptor (ANP-A receptor)	3589 3546*3547ins GAAA	F
X16087	X16087	272750	GEN-1XG	Human mRNA for G(M2) activator protein	13 13A>G	T5A
X16087	X16087	272750	GEN-1XG	Human mRNA for G(M2) activator protein	133 133G>A	V45I
X16087	X16087	272750	GEN-1XG	Human mRNA for G(M2) activator protein	163 163G>A	V55M
PACE	X17094	136950	GEN-1ZV	Human fur mRNA for furin	399 183C>T	S
PACE	X17094	136950	GEN-1ZV	Human fur mRNA for furin	1692 1476C>T	S
PACE	X17094	136950	GEN-1ZV	Human fur mRNA for furin	2067 1851C>G	S
PACE	X17094	136950	GEN-1ZV	Human fur mRNA for furin	2725 2509T>C	3
PACE	X17094	136950	GEN-1ZV	Human fur mRNA for furin	2855 2639C>A	3
PACE	X17094	136950	GEN-1ZV	Human fur mRNA for furin	2988 2772G>A	3
PACE	X17094	136950	GEN-1ZV	Human fur mRNA for furin	3234 3018C>T	3
PACE	X17094	136950	GEN-1ZV	Human fur mRNA for furin	3625 3409A>G	3
PACE	X17094	136950	GEN-1ZV	Human fur mRNA for furin	3883 3667C>T	3
PACE	X17094	136950	GEN-1ZV	Human fur mRNA for furin	4053 3837A>G	3
X51362	X51362	126450	GEN-	Dopamine Receptor D2	588 423G>A	S

X51362	X51362	126450	31W GEN-	Dopamine Receptor D2	1104 939C>T	S
X51362	X51362	126450	31W GEN-	Dopamine Receptor D2	1122 957T>C	S
X51362	X51362	126450	31W GEN-	Dopamine Receptor D2	1248 1083A>G	S
X51362	X51362	126450	31W GEN-	Dopamine Receptor D2	1488 1323T>C	S
X51362	X51362	126450	31W GEN-	Dopamine Receptor D2	1548 1383A>G	3
X51362	X51362	126450	31W GEN-	Dopamine Receptor D2	2361 2196C>T	3
X51416	X51416	601998	31W GEN-57	STEROID HORMONE RECEPTOR ERR1	2285 2222G>A	3
FGFR1	X51803	136350	GEN- 32G	Human mRNA for fibroblast growth factor (FGF) receptor	276 159T>G	S
EDN3	X52001	131242	GEN- 33E	Endothelin 3	1262 1152G>A	3
EDN3	X52001	131242	GEN- 33E	Endothelin 3	1649 1539C>G	3
EDN3	X52001	131242	GEN- 33E	Endothelin 3	1700 1590C>T	3
EDN3	X52001	131242	GEN- 33E	Endothelin 3	1742 1632C>T	3
EDN3	X52001	131242	GEN- 33E	Endothelin 3	1797 1687C>T	3
EDN3	X52001	131242	GEN- 33E	Endothelin 3	1914 1804G>C	3
EDN3	X52001	131242	GEN- 33E	Endothelin 3	2040 1930C>T	3
X52008	X52008	305990	GEN-22	Glycine receptor alpha2	591 204T>G	S
GLRA1	X52009	138491	GEN-4FJ	H.sapiens alpha-1 strychnine binding subunit of inhibitory glycine receptor mRNA	1477 1181C>T	P394L
GLRA1	X52009	138491	GEN-4FJ	H.sapiens alpha-1 strychnine binding subunit of inhibitory glycine receptor mRNA	1520 1224C>T	S

X52479	X52479	176960	GEN-LM	Protein kinase C, alpha	908 881A>C	D294A
NGFB	X52599	162030	GEN-33V	Human mRNA for beta nerve growth factor	832 663G>A	S
PDHA1	X52709	312170	GEN-33Y	Human mRNA for brain pyruvate dehydrogenase (EC 1.2.4.1)	849 795A>G	S
PDHA1	X52709	312170	GEN-33Y	Human mRNA for brain pyruvate dehydrogenase (EC 1.2.4.1)	1337 1283C>T	3
PDHA1	X52709	312170	GEN-33Y	Human mRNA for brain pyruvate dehydrogenase (EC 1.2.4.1)	1416 1362G>A	3
X52773	X52773	180245	GEN-74	Retinoid X receptor, alpha	1744 1669G>A	3
FGFR2	X52832	176943	GEN-341	Human bek mRNA for fibroblast growth factor receptor-BEK	338 159A>G	S
FGFR2	X52832	176943	GEN-341	Human bek mRNA for fibroblast growth factor receptor-BEK	2903 2724A>T	3
CHRNA3	X53559	118503	GEN-34I	Nicotinic, Cholinergic receptor alpha 3	212 212A>G	D71G
CHRNA3	X53559	118503	GEN-34I	Nicotinic, Cholinergic receptor alpha 3	552 552C>T	S
X54199	X54199	138440	GEN-LS	Phosphoribosylglycinamide formyltransferase, phosphoribosylglycinamide synthetase, phosphoribosylaminimidazole synthetase	168 90G>A	S
X54315	X54315	114020	GEN-351	Human mRNA for N-cadherin	2549 2448T>C	S
AGXT	X56092	259900	GEN-36R	Human Ser-PyrAT mRNA for serine-pyruvate aminotransferase	1234 1213C>A	3
FGFR4	X57205	134935	GEN-37M	Human FGFR-4 mRNA for fibroblast growth factor receptor (FGFR-4)	83 28G>A	V10I
FGFR4	X57205	134935	GEN-37M	Human FGFR-4 mRNA for fibroblast growth factor receptor (FGFR-4)	217 162T>G	S
YWHAB	X57346	601289	GEN-	H.sapiens mRNA for HS1	432 60C>A	S

YWHAB	X57346	601289	37R GEN-	H.sapiens mRNA for HS1 protein	1135 763T>C	3
X57348	X57348	601290	37R GEN-	H.sapiens mRNA (clone 9112)	1317 1152C>T	3
X57348	X57348	601290	37S GEN-	H.sapiens mRNA (clone 9112)	1342 1177C>T	3
X57830	X57830	182135	37S GEN-7V	Serotonin 5-HT2 receptor	247 102T>C	S
CRHBP	X58022	122559	38K GEN-	Human mRNA for corticotropin-releasing factor binding protein (CRF-BP)	987 941T>G	I314S
DRD1	X58987	126449	4EH GEN-	D1 dopaminergic receptor	229 (-48)A>G	5
DRD1	X58987	126449	4EH GEN-	D1 dopaminergic receptor	366 90G>A	S
DRD1	X58987	126449	4EH GEN-	D1 dopaminergic receptor	474 198G>A	S
DRD1	X58987	126449	4EH GEN-	D1 dopaminergic receptor	1539 1263G>A	S
X59834	X59834	138290	4EH GEN-M4	Glutamate-ammonia ligase (glutamine synthase)	67 (-43)G>C	5
X59834	X59834	138290	GEN-M4	Glutamate-ammonia ligase (glutamine synthase)	304 195T>C	S
X59834	X59834	138290	GEN-M4	Glutamate-ammonia ligase (glutamine synthase)	1127 1018C>T	R340C
X59834	X59834	138290	GEN-M4	Glutamate-ammonia ligase (glutamine synthase)	2048 1939G>A	3
X59834	X59834	138290	GEN-M4	Glutamate-ammonia ligase (glutamine synthase)	2694 2585C>G	3
X59847	X59847	308840	GEN-3A5	H.sapiens mRNA for neural cell adhesion molecule L1	855 855C>T	S
X61157	X61157	109635	GEN-23	Adrenergic receptor (Beta kinase 1-phosphorylates beta adrenergic receptor)	203 96A>C	S
X61157	X61157	109635	GEN-23	Adrenergic receptor (Beta kinase 1-phosphorylates beta adrenergic receptor)	1372 1265A>G	H422R
X61157	X61157	109635	GEN-23	Adrenergic receptor (Beta kinase 1-phosphorylates beta adrenergic receptor)	1501 1394G>A	R465K

X61157	X61157	109635	GEN-23	Adrenergic receptor (Beta kinase 1-phosphorylates beta adrenergic receptor)	1766 1659C>T	S
X61157	X61157	109635	GEN-23	Adrenergic receptor (Beta kinase 1-phosphorylates beta adrenergic receptor)	1823 1716T>C	S
X61157	X61157	109635	GEN-23	Adrenergic receptor (Beta kinase 1-phosphorylates beta adrenergic receptor)	2976 2869G>A	3
X63368	X63368	604139	GEN-MD	DNAJ PROTEIN	2593 2568C>A	3
X63522	X63522	180246	GEN-75	HOMOLOG HSJ1	1331 1152T>C	S
X64878	X64878	167055	GEN-24	MHC class I promoter binding protein	4048 3681A>C	3
X65019	X65019	147678	GEN-6G	Oxytocin receptor	51 44G>A	R15H
X65019	X65019	147678	GEN-6G	INTERLEUKIN 1 BETA CONVERTASE		
X65019	X65019	147678	GEN-6G	INTERLEUKIN 1 BETA CONVERTASE	116 109A>C	K37Q
X65019	X65019	147678	GEN-6G	INTERLEUKIN 1 BETA CONVERTASE	261 254G>A	G85E
NTRK1	X66397	191315	GEN-3GN	PRECUSOR	2632 2335G>A	V779I
X66403	X66403	100725	GEN-5D	H.sapiens tpr mRNA	2236 2225G>T	3
X66403	X66403	100725	GEN-5D	Nicotinic, Cholinergic receptor epsilon polypeptide	2333 2322A>G	3
X66403	X66403	100725	GEN-5D	Nicotinic, Cholinergic receptor epsilon polypeptide	2364 2353G>T	3
X69117	X69117	109636	GEN-5G	Nicotinic, Cholinergic receptor epsilon polypeptide	1182 1182T>C	S
X69117	X69117	109636	GEN-5G	BETA-ADRENERGIC RECEPTOR KINASE 2	1609 1609G>A	E537K
X70811	X70811	109691	GEN-3KK	BETA-ADRENERGIC RECEPTOR KINASE 2	315 190T>C	W64R
X71490	X71490	108746	GEN-MX	beta-3-adrenergic receptor ATPase, H+ transporting,	1247 991C>A	3

X71490	X71490	108746	GEN-MX	lysosomal (vacuolar proton pump) 31kD	1555	1299C>A	3
NOS2A	X73029	163730	GEN-3LW	ATPase, H+ transporting, lysosomal (vacuolar proton pump) 31kD	1380	1155C>T	S
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	1503	1278C>T	S
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	2048	1823C>T	S608L
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	2287	2062G>A	G688S
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	2339	2114A>G	D705G
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	2583	2358T>C	S
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	2982	2757A>G	S
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	3022	2797C>G	R933G
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	3051	2826C>T	S
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	3693	3468T>C	3
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	3715	3490G>A	3
PREP	X74496	600400	GEN-3N8	H.sapiens mRNA for nitric oxide synthase	390	390T>C	S
PREP	X74496	600400	GEN-3N8	Prolyl Endopeptidase	1051	1051T>G	L351V
PREP	X74496	600400	GEN-3N8	Prolyl Endopeptidase	1125	1125C>T	S
PREP	X74496	600400	GEN-3N8	Prolyl Endopeptidase	1363	1363G>A	V455M
X75299	X75299	192321	GEN-3NU	H.sapiens HIVR mRNA for vasoactive intestinal peptide (VIP) receptor	1915	1904T>C	3
X75299	X75299	192321	GEN-3NU	H.sapiens HIVR mRNA for vasoactive intestinal peptide (VIP) receptor	2475	2464T>C	3

X75958	X75958	600456	GEN-3OE	H.sapiens trkB mRNA for protein-tyrosine kinase	30 (-68)C>G	5
X75958	X75958	600456	GEN-3OE	H.sapiens trkB mRNA for protein-tyrosine kinase	2010 1913A>G	3
X75958	X75958	600456	GEN-3OE	H.sapiens trkB mRNA for protein-tyrosine kinase	2101 2004C>T	3
X76228	X76228	108746	GEN-N6	ATPase, H+ transporting, lysosomal (vacuolar proton pump) 31kD	46 (-30)G>A	5
X76228	X76228	108746	GEN-N6	ATPase, H+ transporting, lysosomal (vacuolar proton pump) 31kD	1023 948A>G	3
X76228	X76228	108746	GEN-N6	ATPase, H+ transporting, lysosomal (vacuolar proton pump) 31kD	1143 1068C>T	3
LIPA	X76488	278000	GEN-3P2	H.sapiens mRNA for lysosomal acid lipase	191 46A>C	T16P
LIPA	X76488	278000	GEN-3P2	H.sapiens mRNA for lysosomal acid lipase	212 67G>A	G23R
LIPA	X76488	278000	GEN-3P2	H.sapiens mRNA for lysosomal acid lipase	967 822G>A	M274I
LIPA	X76488	278000	GEN-3P2	H.sapiens mRNA for lysosomal acid lipase	1531 1386C>T	3
LIPA	X76488	278000	GEN-3P2	H.sapiens mRNA for lysosomal acid lipase	2254 2109A>T	3
LIPA	X76488	278000	GEN-3P2	H.sapiens mRNA for lysosomal acid lipase	2439 2294C>T	3
NMB	X76534	162340	GEN-3P5	H.sapiens NMB mRNA	481 390A>G	S
NMB	X76534	162340	GEN-3P5	H.sapiens NMB mRNA	2478 2387T>C	3
NMB	X76534	162340	GEN-3P5	H.sapiens NMB mRNA	2655 2564A>C	3
MPV17	X76538	600945	GEN-3P6	H.sapiens Mpv17 mRNA	575 548C>T	3
X77130	X77130	602548	GEN-4FN	H.sapiens mRNA for ORL1 receptor	528 351G>A	S
X77130	X77130	602548	GEN-4FN	H.sapiens mRNA for ORL1 receptor	569 392A>G	Y131C
X77130	X77130	602548	GEN-4FN	H.sapiens mRNA for ORL1 receptor	687 510C>T	S

X77130	X77130	602548	GEN-4FN	H.sapiens mRNA for ORL1 receptor	1303 1126C>G	3
X77130	X77130	602548	GEN-4FN	H.sapiens mRNA for ORL1 receptor	1816 1639G>T	3
CLCN4	X77197	302910	GEN-3PO	H.sapiens mRNA for chloride channel	212 (-172)C>T	5
X77533	X77533	602730	GEN-3Q3	H.sapiens mRNA for activin type II receptor	1462 1458C>T	S
X77722	X77722	602376	GEN-29	Interferon (alpha,beta, omega) receptor 2 (splice variant)	253 28G>T	V10F
X77722	X77722	602376	GEN-29	Interferon (alpha,beta, omega) receptor 2 (splice variant)	1128 903A>G	S
X77748	X77748	601115	GEN-3QD	Metabotropic glutamate receptor type 3	384 126G>A	S
YWHAH	X78138	113508	GEN-3QU	H.sapiens 14-3-3 eta subtype mRNA	953 753A>G	3
YWHAH	X78138	113508	GEN-3QU	H.sapiens 14-3-3 eta subtype mRNA	960 760G>A	3
YWHAH	X78138	113508	GEN-3QU	H.sapiens 14-3-3 eta subtype mRNA	1387 1187C>T	3
X78282	X78282	601292	GEN-LVF	H.sapiens mRNA for aryl sulfotransferase (ST1A2)	895 895T>C	3
X78520	X78520	600580	GEN-3RG	H. sapiens RNA for CLCN3	2804 2142T>C	S
X78520	X78520	600580	GEN-3RG	H. sapiens RNA for CLCN3	2822 2160A>G	S
X78706	X78706	600184	GEN-2A	Carnitine Acetyltransferase	1922 1922G>A	3
X78706	X78706	600184	GEN-2A	Carnitine Acetyltransferase	2378 2378G>A	3
X78706	X78706	600184	GEN-2A	Carnitine Acetyltransferase	2382 2382G>A	3
X80818	X80818	604100	GEN-3VD	Metabotropic glutamate receptor type 4	1625 1455T>C	S
X80818	X80818	604100	GEN-3VD	Metabotropic glutamate receptor type 4	3060 2890A>G	3
X83378	X83378	602726	GEN-NI	Putative Chloride Channel	3181 3155T>G	3
X83378	X83378	602726	GEN-NI	Putative Chloride Channel	5041 5015G>A	3
X83378	X83378	602726	GEN-NI	Putative Chloride Channel	5366 5340G>A	3
X83861	X83861	176806	GEN-5H	Prostaglandin E receptor 3 (subtype EP3) (alternative)	387 180C>G	S

X86681	X86681	602110	GEN-41E	H.sapiens mRNA for nucleolar protein, HNP36	1725 1340G>A	3
X94552	X94552	604101	GEN-4FW	H.sapiens mRNA for metabotropic glutamate receptor type 7	2027 1789C>T	S
X94552	X94552	604101	GEN-4FW	H.sapiens mRNA for metabotropic glutamate receptor type 7	2434 2196C>T	S
X94552	X94552	604101	GEN-4FW	H.sapiens mRNA for metabotropic glutamate receptor type 7	2473 2235G>A	S
X97058	X97058	602451	GEN-4BB	P2 purinoceptor (P2Y6)	121 (-156)T>G	5
X97370	X97370	601459	GEN-4BM	H.sapiens mRNA for prepronociceptin	167 144T>C	S
X97370	X97370	601459	GEN-4BM	H.sapiens mRNA for prepronociceptin	637 614C>A	3
X97370	X97370	601459	GEN-4BM	H.sapiens mRNA for prepronociceptin	862 839C>G	3
Y00052	Y00052	123840	GEN-SX	Cyclophilin A	221 207C>G	S
Y00052	Y00052	123840	GEN-SX	Cyclophilin A	268 254A>G	D85G
Y00052	Y00052	123840	GEN-SX	Cyclophilin A	332 318C>T	S
Y00052	Y00052	123840	GEN-SX	Cyclophilin A	627 613C>A	3
CHGB	Y00064	118920	GEN-SZ	Human mRNA for secretogranin I (chromogranin B)	2230 2118A>C	3
Y00285	Y00285	147280	GEN-6I	IGF-2 receptor	4613 4466G>A	S1489N
Y00285	Y00285	147280	GEN-6I	IGF-2 receptor	6371 6224C>T	T2075M
Y00285	Y00285	147280	GEN-6I	IGF-2 receptor	6813 6666C>T	S
Y00285	Y00285	147280	GEN-6I	IGF-2 receptor	7150 7003G>A	V2335M
Y00285	Y00285	147280	GEN-6I	IGF-2 receptor	8685 8538C>A	3
Y00749	Y00749	131240	GEN-P7	Endothelin 1	846 594G>T	K198N
Y08110	Y08110	602005	GEN-1FK	H.sapiens mRNA for mosaic protein LR11	3641 3561T>G	S
Y08110	Y08110	602005	GEN-1FK	H.sapiens mRNA for mosaic protein LR11	3818 3738C>T	S
Y08110	Y08110	602005	GEN-1FK	H.sapiens mRNA for mosaic protein LR11	5158 5078G>A	S1693N

Y08110	Y08110	602005	GEN-1FK	H.sapiens mRNA for mosaic protein LR11	6571 6491G>A	R2164K
Y08756	Y08756	602164	GEN-4EC	Serotonin 5-HT receptors	765 747T>C	S
Y09561	Y09561	None	GEN-4F4	H.sapiens mRNA for P2X7 receptor	835 809A>G	H270R
Y09561	Y09561	None	GEN-4F4	H.sapiens mRNA for P2X7 receptor	946 920G>A	R307Q
Y09561	Y09561	None	GEN-4F4	H.sapiens mRNA for P2X7 receptor	1068 1042G>A	A348T
Y09561	Y09561	None	GEN-4F4	H.sapiens mRNA for P2X7 receptor	1096 1070C>G	T357S
Y09561	Y09561	None	GEN-4F4	H.sapiens mRNA for P2X7 receptor	1405 1379A>G	Q460R
Y09561	Y09561	None	GEN-4F4	H.sapiens mRNA for P2X7 receptor	1589 1563C>G	H521Q
Y09561	Y09561	None	GEN-4F4	H.sapiens mRNA for P2X7 receptor	1590 1564G>A	V522I
Y09561	Y09561	None	GEN-4F4	H.sapiens mRNA for P2X7 receptor	1628 1602G>T	S
Y09561	Y09561	None	GEN-4F4	H.sapiens mRNA for P2X7 receptor	1759 1733G>A	R578Q
Y09561	Y09561	None	GEN-4F4	H.sapiens mRNA for P2X7 receptor	1772 1746G>A	S
Y09567	Y09567	602534	GEN-1H3	Homo sapiens mRNA for SNAP23A protein, complete CDS	396 396G>A	S
Y09765	Y09765	300093	GEN-2C	Gamma-aminobutyric acid (GABA) A receptor	358 304T>G	S102A
Y09765	Y09765	300093	GEN-2C	Gamma-aminobutyric acid (GABA) A receptor	1768 1714T>C	3
Y09765	Y09765	300093	GEN-2C	Gamma-aminobutyric acid (GABA) A receptor	1768 1714T>C	3
Y09765	Y09765	300093	GEN-2C	Gamma-aminobutyric acid (GABA) A receptor	1976 1922C>T	3
Y09765	Y09765	300093	GEN-2C	Gamma-aminobutyric acid (GABA) A receptor	1976 1922C>T	3
Y09765	Y09765	300093	GEN-2C	Gamma-aminobutyric acid (GABA) A receptor	2470 2416T>C	3
Y09765	Y09765	300093	GEN-2C	Gamma-aminobutyric acid (GABA) A receptor	2499 2445A>G	3

Y11044	Y11044	603540	GEN-1JS	Homo sapiens mRNA for GABA-BR1a (hGB1a) receptor	60 61G>T	3
Y12226	Y12226	603533	GEN-1LV	H.sapiens mRNA for gamma-adaptin	3264 3236T>C	3
Y12226	Y12226	603533	GEN-1LV	H.sapiens mRNA for gamma-adaptin	3569 3541T>C	3
Y12226	Y12226	603533	GEN-1LV	H.sapiens mRNA for gamma-adaptin	3683 3655A>G	3
Y15286	Y15286	None	GEN-1TU	Homo sapiens mRNA for vacuolar proton-ATPase subunit M9.2	40 (-23)G>A	5
Y15521	Y15521	None	GEN-MEN	Homo sapiens ASMTL gene	1622 1622A>G	K541R
Z15108	Z15108	176982	GEN-1TE	H.sapiens mRNA for protein kinase C zeta	246 240T>C	S
Z15108	Z15108	176982	GEN-1TE	H.sapiens mRNA for protein kinase C zeta	1694 1688A>C	D563A
Z15108	Z15108	176982	GEN-1TE	H.sapiens mRNA for protein kinase C zeta	2033 2027G>A	3
Z15108	Z15108	176982	GEN-1TE	H.sapiens mRNA for protein kinase C zeta	2086 2080T>G	3
Z26649	Z26649	600230	GEN-2B5	Phospholipase C beta-3	437 438C>T	3
Z26649	Z26649	600230	GEN-2B5	Phospholipase C beta-3	466 467G>A	3
Z26649	Z26649	600230	GEN-2B5	Phospholipase C beta-3	2664 2665C>T	3
Z31357	Z31357	603943	GEN-2GM	H.sapiens mRNA for cysteine dioxygenase type 1	388 134T>C	I45T
ECE1	Z35307	600423	GEN-2MA	Endothelin Converting Enzyme 1	1141 1104C>T	S
ECE1	Z35307	600423	GEN-2MA	Endothelin Converting Enzyme 1	1627 1590T>C	S
ECE1	Z35307	600423	GEN-2MA	Endothelin Converting Enzyme 1	1696 1659G>A	S
ECE1	Z35307	600423	GEN-2MA	Endothelin Converting Enzyme 1	1946 1909G>A	V637M
ECE1	Z35307	600423	GEN-2MA	Endothelin Converting Enzyme 1	2433 2396G>A	3

PDE4C	Z46632	600128	GEN-2X2	H.sapiens HSPDE4C1 gene for 3,5-cyclic AMP phosphodiesterase	280 169C>T	R57C
PDE4C	Z46632	600128	GEN-2X2	H.sapiens HSPDE4C1 gene for 3,5-cyclic AMP phosphodiesterase	1142 1031G>A	R344Q
Z69028	Z69028	601644	GEN-3J4	H.sapiens mRNA for beta 2 isoform of 61 kDa regulatory subunit of PP2A	1681 1612A>T	3
PAM	M37721	170270	GEN-2OK	Human peptidylglycine alpha-amidating monooxygenase mRNA, complete cds	3183 2995T>A	3
PAM	M37721	170270	GEN-2OK	Human peptidylglycine alpha-amidating monooxygenase mRNA, complete cds	3530 3342A>G	3
PACE	X17094	136950	GEN-1ZV	Human fur mRNA for furin	399 183C>T	S
PACE	X17094	136950	GEN-1ZV	Human fur mRNA for furin	1692 1476C>T	S
PACE	X17094	136950	GEN-1ZV	Human fur mRNA for furin	2067 1851C>G	S
PACE	X17094	136950	GEN-1ZV	Human fur mRNA for furin	2725 2509T>C	3
PACE	X17094	136950	GEN-1ZV	Human fur mRNA for furin	2855 2639C>A	3
PACE	X17094	136950	GEN-1ZV	Human fur mRNA for furin	2988 2772G>A	3
PACE	X17094	136950	GEN-1ZV	Human fur mRNA for furin	3234 3018C>T	3
PACE	X17094	136950	GEN-1ZV	Human fur mRNA for furin	3625 3409A>G	3
PACE	X17094	136950	GEN-1ZV	Human fur mRNA for furin	3883 3667C>T	3
PACE	X17094	136950	GEN-1ZV	Human fur mRNA for furin	4053 3837A>G	3

Table 14.
Identified
Variances

In Genes
and
Related
Pathways
Identified
in
Pharmacokinetic
and
Pharmacodynamic
Parameters of
Candidate
Therapeutic
Interventions

AAC2	D90040	243400	GEN-465	Human mRNA for arylamine N- acetyltransferase (EC 2.3.1.5)	232	191G>A	R64Q
AAC2	D90040	243400	GEN-465	Human mRNA for arylamine N- acetyltransferase (EC 2.3.1.5)	323	282C>T	S
AAC2	D90040	243400	GEN-465	Human mRNA for arylamine N- acetyltransferase (EC 2.3.1.5)	844	803A>G	K268R
AB00081	AB00081	602550	GEN-14E	Human mRNA for BMAL1b, complete cds	1084	1044C>A	S
AB00379	AB00379	603797	GEN-1F9	Homo sapiens mRNA for keratan sulfate Gal-6- sulfotransferase, complete cds	1617	1251G>A	3
AB00379	AB00379	603797	GEN-1F9	Homo sapiens mRNA for keratan sulfate Gal-6- sulfotransferase, complete cds	1643	1277G>A	3

AB00485	AB00485	603608	GEN- KV6	Homo sapiens mRNA for carbonyl reductase 3, complete cds	730	730G>A	V244M
AB00528	AB00528	300135	GEN- KVU	Homo sapiens mRNA for ABC transporter 7 protein, complete cds	2137	2069A>T	H690L
AB01467	AB01467	None	GEN-L22	Homo sapiens GN6ST mRNA for N- acetylglucosamine-6-O- sulfotransferase (GlcNAc6ST), complete cds	1578	1189G>T	V397L
AB01467	AB01467	None	GEN-L22	Homo sapiens GN6ST mRNA for N- acetylglucosamine-6-O- sulfotransferase (GlcNAc6ST), complete cds	2335	1946T>C	3
AB01505	AB01505	603377	GEN- L2D	Homo sapiens mRNA for OCTN2, complete cds	1101	978G>A	S
ABC3	X97187	601615	GEN-4BI	H.sapiens mRNA for ABC- C transporter	4671	4324G>T	V1442F
ABC3	X97187	601615	GEN-4BI	H.sapiens mRNA for ABC- C transporter	5075	4728G>A	S
ADH2	M24317	103720	GEN- 28A	Human class I alcohol dehydrogenase (ADH2) beta-1 subunit mRNA, complete cds	817	787G>A	V263M
ADH3	M12272	103730	GEN- 1LU	Homo sapiens alcohol dehydrogenase class I gamma subunit (ADH3) mRNA, complete cds	1128	1048A>G	I350V
ADH4	M15943	103740	GEN- 1UM	Human class II alcohol dehydrogenase (ADH4) pi subunit mRNA, complete cds	826	765G>T	S
ADH4	M15943	103740	GEN- 1UM	Human class II alcohol dehydrogenase (ADH4) pi subunit mRNA, complete cds	1389	1328T>C	3
ADH5	M29872	103710	GEN-	Human alcohol	1029	1025G>A	S342N

ADH5	M29872	103710	2EU	dehydrogenase class III (ADH5) mRNA, complete cds	1375	1371T>C	3
AF001437	AF001437	245349	GEN- 2EU	Human alcohol dehydrogenase class III (ADH5) mRNA, complete cds	75	67T>C	C23R
AF001437	AF001437	245349	GEN-9T	Dihydrolipoamide S- acetyltransferase (E2 component of pyruvate dehydrogenase complex)	116	108C>T	S
AF001437	AF001437	245349	GEN-9T	Dihydrolipoamide S- acetyltransferase (E2 component of pyruvate dehydrogenase complex)	759	751T>G	S251A
AF001437	AF001437	245349	GEN-9T	Dihydrolipoamide S- acetyltransferase (E2 component of pyruvate dehydrogenase complex)	806	798C>T	S
AF001437	AF001437	245349	GEN-9T	Dihydrolipoamide S- acetyltransferase (E2 component of pyruvate dehydrogenase complex)	866	858T>C	S
AF001437	AF001437	245349	GEN-9T	Dihydrolipoamide S- acetyltransferase (E2 component of pyruvate dehydrogenase complex)	2000	1992G>T	3
AF001437	AF001437	245349	GEN-9T	Dihydrolipoamide S- acetyltransferase (E2 component of pyruvate dehydrogenase complex)	2158	2150C>A	3
AF001945	AF001945	601691	GEN- 17Z	Homo sapiens rim ABC transporter (ABCR) mRNA, complete cds	2725	2644G>A	G882S
AF001945	AF001945	601691	GEN- 17Z	Homo sapiens rim ABC transporter (ABCR) mRNA, complete cds	5136	5055C>T	S

AF009746	AF009746	603214	GEN-1HZ	Homo sapiens peroxisomal membrane protein 69 (PMP69) mRNA, complete cds	961	910G>A	A304T
AF009746	AF009746	603214	GEN-1HZ	Homo sapiens peroxisomal membrane protein 69 (PMP69) mRNA, complete cds	1895	1844A>G	3
AF009746	AF009746	603214	GEN-1HZ	Homo sapiens peroxisomal membrane protein 69 (PMP69) mRNA, complete cds	2134	2083T>G	3
AF019386	AF019386	None	GEN-231	Homo sapiens heparan sulfate 3-O-sulfotransferase-1 precursor (3OST1) mRNA, complete cds	79	(-40)C>G	5
AF026947	AF026947	603418	GEN-261	Homo sapiens aflatoxin aldehyde reductase AFAR mRNA, complete cds	1013	936T>C	S
AF026947	AF026947	603418	GEN-261	Homo sapiens aflatoxin aldehyde reductase AFAR mRNA, complete cds	1078	1001A>G	3
AF027302	AF027302	603429	GEN-27T	Homo sapiens TNF-alpha stimulated ABC protein (ABC50) mRNA, complete cds	3075	2981T>C	3
AF028738	AF028738	602631	GEN-2F6	Homo sapiens imprinted multi-membrane spanning polyspecific transporter-related protein (IMPT1) mRNA, complete cds	34	(-209)A>C	5
AF028738	AF028738	602631	GEN-2F6	Homo sapiens imprinted multi-membrane spanning polyspecific transporter-related protein (IMPT1) mRNA, complete cds	210	(-33)G>A	5
AF028738	AF028738	602631	GEN-2F6	Homo sapiens imprinted multi-membrane spanning polyspecific transporter-related protein (IMPT1) mRNA, complete cds	229	(-14)A>G	5

AF028738	AF028738	602631	GEN- 2F6	mRNA, complete cds Homo sapiens imprinted multi-membrane spanning polyspecific transporter- related protein (IMPT1)	375	133T>G	F45V
AF028738	AF028738	602631	GEN- 2F6	mRNA, complete cds Homo sapiens imprinted multi-membrane spanning polyspecific transporter- related protein (IMPT1)	875	633A>C	E211D
AF028738	AF028738	602631	GEN- 2F6	mRNA, complete cds Homo sapiens imprinted multi-membrane spanning polyspecific transporter- related protein (IMPT1)	881	639A>G	S
AF028738	AF028738	602631	GEN- 2F6	mRNA, complete cds Homo sapiens imprinted multi-membrane spanning polyspecific transporter- related protein (IMPT1)	883	641G>C	G214A
AF028738	AF028738	602631	GEN- 2F6	mRNA, complete cds Homo sapiens imprinted multi-membrane spanning polyspecific transporter- related protein (IMPT1)	919	677A>G	K226R
AF028738	AF028738	602631	GEN- 2F6	mRNA, complete cds Homo sapiens imprinted multi-membrane spanning polyspecific transporter- related protein (IMPT1)	927	685T>C	S
AF028738	AF028738	602631	GEN- 2F6	mRNA, complete cds Homo sapiens imprinted multi-membrane spanning polyspecific transporter- related protein (IMPT1)	935	693A>G	S
AF028738	AF028738	602631	GEN- 2F6	mRNA, complete cds Homo sapiens imprinted multi-membrane spanning polyspecific transporter- related protein (IMPT1)	1004	762A>G	S

AF028738	AF028738	602631	GEN- 2F6	Homo sapiens imprinted multi-membrane spanning polyspecific transporter-related protein (IMPT1) mRNA, complete cds	1017	775A>C	K259Q
AF028738	AF028738	602631	GEN- 2F6	Homo sapiens imprinted multi-membrane spanning polyspecific transporter-related protein (IMPT1) mRNA, complete cds	1106	864A>G	S
AF028738	AF028738	602631	GEN- 2F6	Homo sapiens imprinted multi-membrane spanning polyspecific transporter-related protein (IMPT1) mRNA, complete cds	1119	877G>C	G293R
AF028738	AF028738	602631	GEN- 2F6	Homo sapiens imprinted multi-membrane spanning polyspecific transporter-related protein (IMPT1) mRNA, complete cds	1124	882A>C	S
AF028738	AF028738	602631	GEN- 2F6	Homo sapiens imprinted multi-membrane spanning polyspecific transporter-related protein (IMPT1) mRNA, complete cds	1166	924G>C	W308C
AF038175	AF038175	None	GEN- 2QM	Homo sapiens clone 23819 white protein homolog mRNA, partial cds	1100	1100G>A	3
AF055025	AF055025	300095	GEN- 32U	Homo sapiens clone 24776 mRNA sequence	784	785A>G	3
AF055025	AF055025	300095	GEN- 32U	Homo sapiens clone 24776 mRNA sequence	2021	2022A>T	3
AF058056	AF058056	None	GEN- MNJ	Homo sapiens monocarboxylate transporter 2 (hMCT2) mRNA, complete cds	200	73G>A	A25T
AF058056	AF058056	None	GEN- MNJ	Homo sapiens monocarboxylate transporter 2 (hMCT2) mRNA, complete cds	203	76G>A	A26T
AF058056	AF058056	None	GEN-	Homo sapiens mRNA, complete cds	588	461G>A	S154N

SD-144146.1

AJ130718	AJ130718	None	GEN- LDO	Homo sapiens mRNA for glycoprotein-associated amino acid transporter y ⁺ -LAT1	1820	1527G>A	S
ALDH10	L47162	270200	GEN-2XI	Human fatty aldehyde dehydrogenase (FALDH) mRNA, complete cds	1609	1446A>T	S
ALDH3	M74542	100660	GEN- 3N9	Human aldehyde dehydrogenase type III (ALDHIII) mRNA, complete cds	1616	1574A>G	3
ALDH6	U07919	600463	GEN- 1F5	Human aldehyde dehydrogenase 6 mRNA, complete cds	2453	2401A>G	3
ALDH6	U07919	600463	GEN- 1F5	Human aldehyde dehydrogenase 6 mRNA, complete cds	3396	3344C>T	3
ALDH6	U07919	600463	GEN- 1F5	Human aldehyde dehydrogenase 6 mRNA, complete cds	3397	3345G>A	3
ARNT	M69238	126110	GEN- 3JH	Human aryl hydrocarbon receptor nuclear translocator (ARNT) mRNA, complete cds	623	567G>C	S
ARSB	M32373	253200	GEN-2J0	Human arylsulfatase B (ASB) mRNA, complete cds	1631	1072G>A	V358M
ARSE	X83573	300180	GEN- 3Y8	Homo sapiens ARSE gene, complete CDS	1759	1692C>T	S
ARSE	X83573	300180	GEN- 3Y8	Homo sapiens ARSE gene, complete CDS	1795	1728G>A	S
CAT	X04076	115500	GEN- 13P	Human kidney mRNA for catalase	51	(-20)T>C	5
CAT	X04076	115500	GEN- 13P	Human kidney mRNA for catalase	218	148C>T	L50F
CAT	X04076	115500	GEN- 13P	Human kidney mRNA for catalase	1237	1167T>C	S
CAT	X04076	115500	GEN- 13P	Human kidney mRNA for catalase	1325	1255C>T	S
CAT	X04076	115500	GEN- 13P	Human kidney mRNA for catalase	2131	2061A>C	3

CBG	J02943	122500	GEN-Y2	Human corticosteroid binding globulin mRNA, complete cds	106	71A>T	D24V
CBG	J02943	122500	GEN-Y2	Human corticosteroid binding globulin mRNA, complete cds	971	936T>C	S
CBG	J02943	122500	GEN-Y2	Human corticosteroid binding globulin mRNA, complete cds	1229	1194G>A	S
CBR	J04056	114830	GEN-130	Human carbonyl reductase mRNA, complete cds	1060	967G>A	3
CBS	L00972	236200	GEN-UV	Human cystathionine-beta-synthase (CBS) mRNA	1022	1023T>C	3
CBS	L00972	236200	GEN-UV	Human cystathionine-beta-synthase (CBS) mRNA	2001	2002C>T	3
CBS	L00972	236200	GEN-UV	Human cystathionine-beta-synthase (CBS) mRNA	2278	2279G>A	3
CBS	L00972	236200	GEN-UV	Human cystathionine-beta-synthase (CBS) mRNA	2358	2359G>C	3
CBS	L00972	236200	GEN-UV	Human cystathionine-beta-synthase (CBS) mRNA	2524	2525T>C	3
CBS	L00972	236200	GEN-UV	Human cystathionine-beta-synthase (CBS) mRNA	2545	2546C>T	3
CEL	M85201	114841	GEN-404	Human cholesterol esterase mRNA, complete cds	566	558T>C	S
CEL	M85201	114841	GEN-404	Human cholesterol esterase mRNA, complete cds	1306	1298G>A	S433N
CEL	M85201	114841	GEN-404	Human cholesterol esterase mRNA, complete cds	1826	1818C>T	S
CFTR	M28668	602421	GEN-2DF	Human cystic fibrosis mRNA, encoding a presumed transmembrane conductance regulator (CFTR)	2729	2597G>A	C866Y
CFTR	M28668	602421	GEN-2DF	Human cystic fibrosis mRNA, encoding a presumed transmembrane conductance regulator	5826	5694T>C	3

CPA1	X67318	114850	GEN-3HJ	(CFTR) H.sapiens mRNA for procarboxypeptidase A1	172	165G>C	S
CPA1	X67318	114850	GEN-3HJ	H.sapiens mRNA for procarboxypeptidase A1	498	491C>G	T164R
CPA1	X67318	114850	GEN-3HJ	H.sapiens mRNA for procarboxypeptidase A1	629	622G>A	A208T
CRYZ	L13278	123691	GEN-1NZ	Homo sapiens zeta- crystallin/quinone reductase mRNA, complete cds	64	54G>A	S
CRYZ	L13278	123691	GEN-1NZ	Homo sapiens zeta- crystallin/quinone reductase mRNA, complete cds	902	892G>A	V298M
CRYZ	L13278	123691	GEN-1NZ	Homo sapiens zeta- crystallin/quinone reductase mRNA, complete cds	1229	1219A>G	3
CTH	S52028	219500	GEN-33F	cystathionine gamma-lyase {clone HCL-1} (human, liver, mRNA, 1194 nt)	1109	1076T>G	I359S
CYP11B2	D13752	124080	GEN-CCD	Human CYP11B2 gene for steroid 18-hydroxylase, complete cds	1600	1593G>A	3
CYP1B1	U03688	601771	GEN-11Y	Human dioxin-inducible cytochrome P450 (CYP1B1) mRNA, complete cds	488	142C>G	R48G
CYP1B1	U03688	601771	GEN-11Y	Human dioxin-inducible cytochrome P450 (CYP1B1) mRNA, complete cds	701	355G>T	A119S
CYP1B1	U03688	601771	GEN-11Y	Human dioxin-inducible cytochrome P450 (CYP1B1) mRNA, complete cds	2673	2327G>T	3
CYP21	M17252	201910	GEN-201	Human cytochrome P450c21 mRNA, 3 end	224	224G>A	R75H
CYP21	M17252	201910	GEN-201	Human cytochrome P450c21 mRNA, 3 end	330	330C>T	S

CYP21	M17252	201910	GEN-201	Human cytochrome P450c21 mRNA, 3 end	745	745T>C	3
CYP51	U23942	601637	GEN-27K	Human lanosterol 14-demethylase cytochrome P450 (CYP51) mRNA, complete cds	766	644G>A	C215Y
CYP51	U23942	601637	GEN-27K	Human lanosterol 14-demethylase cytochrome P450 (CYP51) mRNA, complete cds	894	772C>T	R258C
CYP51	U23942	601637	GEN-27K	Human lanosterol 14-demethylase cytochrome P450 (CYP51) mRNA, complete cds	912	790C>T	R264W
CYP51	U23942	601637	GEN-27K	Human lanosterol 14-demethylase cytochrome P450 (CYP51) mRNA, complete cds	1476	1354C>T	R452C
CYP51	U23942	601637	GEN-27K	Human lanosterol 14-demethylase cytochrome P450 (CYP51) mRNA, complete cds	1616	1494G>A	S
CYP51	U23942	601637	GEN-27K	Human lanosterol 14-demethylase cytochrome P450 (CYP51) mRNA, complete cds	1836	1714C>A	3
CYP51	U23942	601637	GEN-27K	Human lanosterol 14-demethylase cytochrome P450 (CYP51) mRNA, complete cds	2283	2161G>T	3
CYP51	U23942	601637	GEN-27K	Human lanosterol 14-demethylase cytochrome P450 (CYP51) mRNA, complete cds	2445	2323T>C	3
CYP51	U23942	601637	GEN-27K	Human lanosterol 14-demethylase cytochrome P450 (CYP51) mRNA, complete cds	2507	2385G>A	3
CYP51	U23942	601637	GEN-27K	Human lanosterol 14-demethylase cytochrome P450 (CYP51) mRNA, complete cds	2556	2434T>A	3

CYP51	U23942	601637	GEN-27K	complete cds Human lanosterol 14-demethylase cytochrome P450 (CYP51) mRNA,	2665	2543G>A	3
D13138	D13138	179780	GEN-1NW	complete cds Human mRNA for dipeptidase	566	523T>G	S175A
D17793	D17793	None	GEN-20Q	Human mRNA for KIAA0119 gene, complete cds	66	15G>C	Q5H
D17793	D17793	None	GEN-20Q	Human mRNA for KIAA0119 gene, complete cds	141	90G>A	S
D17793	D17793	None	GEN-20Q	Human mRNA for KIAA0119 gene, complete cds	363	312A>G	S
D17793	D17793	None	GEN-20Q	Human mRNA for KIAA0119 gene, complete cds	980	929G>C	S310T
D87292	D87292	180370	GEN-42Y	Human mRNA for rhodanese, complete cds	816	768C>T	S
D87292	D87292	180370	GEN-42Y	Human mRNA for rhodanese, complete cds	946	898G>A	3
D87845	D87845	602344	GEN-44C	Human mRNA for platelet-activating factor acetylhydrolase 2, complete cds	2299	2096G>A	3
D87845	D87845	602344	GEN-44C	Human mRNA for platelet-activating factor acetylhydrolase 2, complete cds	2332	2129A>G	3
D89078	D89078	601531	GEN-7	P2Y7 purinoceptor	434	(-1284)A>T	5
D89078	D89078	601531	GEN-7	P2Y7 purinoceptor	889	(-829)G>C	5
D89078	D89078	601531	GEN-7	P2Y7 purinoceptor	1156	(-562)G>C	5
D89078	D89078	601531	GEN-7	P2Y7 purinoceptor	2644	927T>C	S
D89078	D89078	601531	GEN-7	P2Y7 purinoceptor	2920	1203A>G	3
D90041	D90041	108345	GEN-464	Human liver arylamine N-acetyltransferase (EC 2.3.1.5) gene	591	445G>A	V149I
D90041	D90041	108345	GEN-464	Human liver arylamine N-	1240	1094C>A	3

DDH1	U05598	600450	GEN-184	acetyltransferase (EC 2.3.1.5) gene Human dihydrodiol dehydrogenase mRNA, complete cds	38	15C>T	S
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	282	259A>T	S87C
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	350	327C>T	S
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	365	342T>C	S
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	464	441G>A	S
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	474	451A>G	M151V
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	532	509A>G	H170R
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	538	515T>A	L172Q
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	689	666T>C	S
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	806	783G>A	S
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	872	849G>T	S
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	952	929T>G	I310S
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	1020	997G>A	3

DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	1035	1012G>A	3
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	1112	1089C>T	3
DHFR	J00140	126060	GEN-4E9	Human dihydrofolate reductase gene	721	679T>A	3
DHFR	J00140	126060	GEN-4E9	Human dihydrofolate reductase gene	721	679T>A	3
DHFR	J00140	126060	GEN-4E9	Human dihydrofolate reductase gene	829	787C>T	3
EHHADH	L07077	261515	GEN-1DF	Human enoyl-CoA: hydratase 3-hydroxyacyl-CoA dehydrogenase (EHHADH) mRNA, complete cds with repeats	1225	1218G>A	S
EHHADH	L07077	261515	GEN-1DF	Human enoyl-CoA: hydratase 3-hydroxyacyl-CoA dehydrogenase (EHHADH) mRNA, complete cds with repeats	1823	1816C>A	P606T
ELA1	M16631	130120	GEN-1YI	Human elastase 2 mRNA, complete cds	510	489G>A	S
ELA1	M16631	130120	GEN-1YI	Human elastase 2 mRNA, complete cds	693	672G>A	S
EPHX1	L25878	132810	GEN-29Z	Homo sapiens p33/HEH epoxide hydrolase (EPHX) mRNA, complete cds	460	337T>C	Y113H
EPHX1	L25878	132810	GEN-29Z	Homo sapiens p33/HEH epoxide hydrolase (EPHX) mRNA, complete cds	480	357A>G	S
EPHX1	L25878	132810	GEN-29Z	Homo sapiens p33/HEH epoxide hydrolase (EPHX) mRNA, complete cds	539	416A>G	H139R
EPHX1	L25878	132810	GEN-29Z	Homo sapiens p33/HEH epoxide hydrolase (EPHX) mRNA, complete cds	1194	1071C>T	S
EPHX2	L05779	132811	GEN-18A	Human cytosolic epoxide hydrolase mRNA, complete cds	1631	1590A>C	S

EPHX2	L05779	132811	GEN-18A	Human cytosolic epoxide hydrolase mRNA, complete cds	1742	1701A>G	3
EPHX2	L05779	132811	GEN-18A	Human cytosolic epoxide hydrolase mRNA, complete cds	1800	1759T>C	3
FABP2	M10050	134640	GEN-11E	Human liver fatty acid binding protein (FABP) mRNA, complete cds	322	280G>A	A94T
FACL1	L09229	152425	GEN-1GI	Human long-chain acyl-coenzyme A synthetase (FACL1) mRNA, complete cds	3026	2953G>A	3
FACL1	L09229	152425	GEN-1GI	Human long-chain acyl-coenzyme A synthetase (FACL1) mRNA, complete cds	3083	3010G>A	3
GC	M12654	139200	GEN-1MN	Human serum vitamin D-binding protein (hDBP) mRNA, complete cds	925	897T>C	S
GC	M12654	139200	GEN-1MN	Human serum vitamin D-binding protein (hDBP) mRNA, complete cds	1324	1296G>T	E432D
GC	M12654	139200	GEN-1MN	Human serum vitamin D-binding protein (hDBP) mRNA, complete cds	1335	1307C>A	T436K
GC	M12654	139200	GEN-1MN	Human serum vitamin D-binding protein (hDBP) mRNA, complete cds	1362	1334G>A	R445H
GPX1	Y00433	138320	GEN-TJ	Human mRNA for glutathione peroxidase (EC 1.11.1.9.)	504	186G>A	S
GPX1	Y00433	138320	GEN-TJ	Human mRNA for glutathione peroxidase (EC 1.11.1.9.)	610	292C>G	R98G
GPX1	Y00433	138320	GEN-TJ	Human mRNA for glutathione peroxidase (EC 1.11.1.9.)	911	593C>T	P198L
GPX1	Y00433	138320	GEN-TJ	Human mRNA for glutathione peroxidase (EC 1.11.1.9.)	1048	730A>C	3

GPX1	Y00433	138320	GEN-TJ	Human mRNA for glutathione peroxidase (EC 1.11.1.9.)	1110	792A>C	3
GPX3	X58295	138321	GEN-38S	Human GPx-3 mRNA for plasma glutathione peroxidase	821	773C>T	3
GPX3	X58295	138321	GEN-38S	Human GPx-3 mRNA for plasma glutathione peroxidase	979	931G>A	3
GPX3	X58295	138321	GEN-38S	Human GPx-3 mRNA for plasma glutathione peroxidase	1187	1139T>G	3
GPX3	X58295	138321	GEN-38S	Human GPx-3 mRNA for plasma glutathione peroxidase	1354	1306C>T	3
GPX3	X58295	138321	GEN-38S	Human GPx-3 mRNA for plasma glutathione peroxidase	1443	1395C>T	3
GPX3	X58295	138321	GEN-38S	Human GPx-3 mRNA for plasma glutathione peroxidase	1516	1468C>A	3
GPX3	X58295	138321	GEN-38S	Human GPx-3 mRNA for plasma glutathione peroxidase	1581	1533C>T	3
GPX4	X71973	138322	GEN-3L1	H.sapiens GPx-4 mRNA for phospholipid hydroperoxide glutathione peroxidase	718	638T>C	3
GPX4	X71973	138322	GEN-3L1	H.sapiens GPx-4 mRNA for phospholipid hydroperoxide glutathione peroxidase	837	757C>A	3
GPX4	X71973	138322	GEN-3L1	H.sapiens GPx-4 mRNA for phospholipid hydroperoxide glutathione peroxidase	882	802A>C	3
GSTM3	J05459	138390	GEN-170	Human glutathione transferase M3 (GSTM3) mRNA, complete cds	687	670G>A	V224I
GSTM5	L02321	138385	GEN-WO	Human glutathione S-transferase (GSTM5)	1406	1349T>C	3

GSTP1	X06547	134660	GEN-19N	mRNA, complete cds Human mRNA for class Pi glutathione S-transferase (GST-Pi; E.C.2.5.1.18)	319	313A>G	I105V
GSTP1	X06547	134660	GEN-19N	Human mRNA for class Pi glutathione S-transferase (GST-Pi; E.C.2.5.1.18)	347	341C>T	A114V
GSTP1	X06547	134660	GEN-19N	Human mRNA for class Pi glutathione S-transferase (GST-Pi; E.C.2.5.1.18)	561	555C>T	S
GSTT2	L38503	600437	GEN-2PC	Homo sapiens glutathione S-transferase theta 2 (GSTT2) mRNA, complete cds	203	203C>T	S68L
GSTT2	L38503	600437	GEN-2PC	Homo sapiens glutathione S-transferase theta 2 (GSTT2) mRNA, complete cds	543	543C>T	S
HADHA	U04627	600890	GEN-155	Human 78 kDa gastrin-binding protein mRNA, complete cds	1507	1507G>A	V503M
HADHB	D16481	143450	GEN-1Y5	Human mRNA for mitochondrial 3-ketoacyl-CoA thiolase beta-subunit of trifunctional protein, complete cds	871	825T>C	S
HADHB	D16481	143450	GEN-1Y5	Human mRNA for mitochondrial 3-ketoacyl-CoA thiolase beta-subunit of trifunctional protein, complete cds	1607	1561G>C	3
HADHB	D16481	143450	GEN-1Y5	Human mRNA for mitochondrial 3-ketoacyl-CoA thiolase beta-subunit of trifunctional protein, complete cds	1908	1862A>C	3
HADHB	D16481	143450	GEN-1Y5	Human mRNA for mitochondrial 3-ketoacyl-CoA thiolase beta-subunit of trifunctional protein, complete cds	1911	1865A>C	3

HRH1	AF026261	600167	GEN-26W	Histamine receptor H1	1068	1068A>G	S
HSST	U17970	600853	GEN-20V	Human heparan sulfate N-deacetylase/N-sulfotransferase mRNA, complete cds	2294	2066G>C	G689A
IDS	L40586	309900	GEN-2SB	Homo sapiens iduronate-2-sulphatase (IDS) mRNA, complete cds	565	438C>T	S
J03459	J03459	151570	GEN-8	Leukotriene A4 hydrolase	140	72G>T	S
J03459	J03459	151570	GEN-8	Leukotriene A4 hydrolase	1511	1443A>T	E481D
J03548	J03548	103260	GEN-11M	Human adrenodoxin mRNA, complete cds	1099	967G>A	3
J03548	J03548	103260	GEN-11M	Human adrenodoxin mRNA, complete cds	1123	991T>C	3
J03548	J03548	103260	GEN-11M	Human adrenodoxin mRNA, complete cds	1222	1090G>C	3
J03548	J03548	103260	GEN-11M	Human adrenodoxin mRNA, complete cds	1254	1122G>A	3
J03571	J03571	152390	GEN-9	Lipoxygenases: 5-lipoxygenase (leukocytes)	55	21C>T	S
J03571	J03571	152390	GEN-9	Lipoxygenases: 5-lipoxygenase (leukocytes)	304	270G>A	S
J03571	J03571	152390	GEN-9	Lipoxygenases: 5-lipoxygenase (leukocytes)	304	270G>A	S
J03571	J03571	152390	GEN-9	Lipoxygenases: 5-lipoxygenase (leukocytes)	959	925C>A	P309T
J03571	J03571	152390	GEN-9	Lipoxygenases: 5-lipoxygenase (leukocytes)	1762	1728A>T	S
J03571	J03571	152390	GEN-9	Lipoxygenases: 5-lipoxygenase (leukocytes)	2076	2042-2043AC>AC	3
J03571	J03571	152390	GEN-9	Lipoxygenases: 5-lipoxygenase (leukocytes)	2076	2042-2043delAC	F
J03571	J03571	152390	GEN-9	Lipoxygenases: 5-lipoxygenase (leukocytes)	2328	2294C>T	3
J03571	J03571	152390	GEN-9	Lipoxygenases: 5-lipoxygenase (leukocytes)	2376	2342T>G	3
J03746	J03746	138330	GEN-11Z	Human glutathione S-transferase mRNA, complete cds	560	487A>G	3
J03746	J03746	138330	GEN-	Human glutathione S-transferase mRNA, complete cds	598	525T>G	3

[illegible]

L02932	L02932	170998	GEN-KW4	polypeptide 1 Human peroxisome proliferator activated receptor mRNA, complete cds	648	432G>A	S
L04751	L04751	601310	GEN-157	Human cytochrome p-450 4A (CYP4A) mRNA, complete cds	1001	969C>T	S
L04751	L04751	601310	GEN-157	Human cytochrome p-450 4A (CYP4A) mRNA, complete cds	1333	1301T>C	F434S
L04751	L04751	601310	GEN-157	Human cytochrome p-450 4A (CYP4A) mRNA, complete cds	1406	1374T>C	S
L04751	L04751	601310	GEN-157	Human cytochrome p-450 4A (CYP4A) mRNA, complete cds	1944	1912A>G	3
L04751	L04751	601310	GEN-157	Human cytochrome p-450 4A (CYP4A) mRNA, complete cds	1970	1938G>A	3
L04751	L04751	601310	GEN-157	Human cytochrome p-450 4A (CYP4A) mRNA, complete cds	2011	1979C>T	3
L04751	L04751	601310	GEN-157	Human cytochrome p-450 4A (CYP4A) mRNA, complete cds	2047	2015T>C	3
L04751	L04751	601310	GEN-157	Human cytochrome p-450 4A (CYP4A) mRNA, complete cds	2115	2083A>G	3
L05628	L05628	158343	GEN-4D9	Human multidrug resistance-associated protein (MRP) mRNA, complete cds	3369	3173G>A	R1058Q
L05628	L05628	158343	GEN-4D9	Human multidrug resistance-associated protein (MRP) mRNA, complete cds	4198	4002G>A	S
L10819	L10819	171150	GEN-LVD	Homo sapiens aryl sulfotransferase mRNA, complete cds	191	153C>T	S
L10819	L10819	171150	GEN-	Homo sapiens aryl complete cds	200	162G>A	S

L10819	L10819	171150	LVD	sulfotransferase mRNA, complete cds	230	192T>C	S
L10819	L10819	171150	GEN-LVD	Homo sapiens aryl sulfotransferase mRNA, complete cds	242	204G>A	S
L10819	L10819	171150	GEN-LVD	Homo sapiens aryl sulfotransferase mRNA, complete cds	295	257C>T	A86V
L10819	L10819	171150	GEN-LVD	Homo sapiens aryl sulfotransferase mRNA, complete cds	330	292G>A	D98N
L10819	L10819	171150	GEN-LVD	Homo sapiens aryl sulfotransferase mRNA, complete cds	338	300G>A	S
L10819	L10819	171150	GEN-LVD	Homo sapiens aryl sulfotransferase mRNA, complete cds	638	600C>G	S
L10819	L10819	171150	GEN-LVD	Homo sapiens aryl sulfotransferase mRNA, complete cds	676	638A>G	H213R
L10819	L10819	171150	GEN-LVD	Homo sapiens aryl sulfotransferase mRNA, complete cds	940	902G>A	3
L10819	L10819	171150	GEN-LVD	Homo sapiens aryl sulfotransferase mRNA, complete cds	1011	973T>C	3
L11696	L11696	104614	GEN-D6	Solute carrier family 3 (cystine, dibasic and neutral amino acid transporters, activator of cystine, dibasic and neutral amino acid transport), member 1	1897	1854G>A	M618I
L11696	L11696	104614	GEN-D6	Solute carrier family 3 (cystine, dibasic and neutral amino acid transporters, activator of cystine, dibasic and neutral amino acid transport), member 1	2232	2189T>C	3

L13286	L13286	600125	GEN-103	Human mitochondrial 1,25-dihydroxyvitamin D3 24-hydroxylase mRNA, complete cds	2031	1638G>A	3
L19956	L19956	600641	GEN-LVE	Human aryl sulfotransferase mRNA, complete cds	243	105A>G	S
L19956	L19956	600641	GEN-LVE	Human aryl sulfotransferase mRNA, complete cds	284	146C>T	S49F
L31801	L31801	600682	GEN-DQ	Solute carrier family 16 (monocarboxylic acid transporters), member 1	1482	1470A>T	E490D
L31801	L31801	600682	GEN-DQ	Solute carrier family 16 (monocarboxylic acid transporters), member 1	1772	1760G>C	3
L32179	L32179	600338	GEN-2IW	Human arylacetamide deacetylase mRNA, complete cds	1366	1281G>A	3
L78207	L78207	600509	GEN-5Q	Cell surface receptor for sulfonyleureas on pancreatic b cells	4019	3981A>G	S
LCT	X07994	603202	GEN-1F6	Human mRNA for lactase-phlorizin hydrolase LPH (EC 3.2.1.23-62)	5845	5834C>G	3
LIPC	J03540	151670	GEN-11J	Human hepatic lipase mRNA, complete cds	469	465T>G	S
LIPC	J03540	151670	GEN-11J	Human hepatic lipase mRNA, complete cds	595	591A>G	S
LIPC	J03540	151670	GEN-11J	Human hepatic lipase mRNA, complete cds	648	644G>A	S215N
LIPC	J03540	151670	GEN-11J	Human hepatic lipase mRNA, complete cds	817	813C>T	S
LIPC	J03540	151670	GEN-11J	Human hepatic lipase mRNA, complete cds	1441	1437C>A	S
M10901	M10901	138040	GEN-2W	Corticosteroid nuclear receptor b	1220	1088A>G	N363S
M10901	M10901	138040	GEN-2W	Corticosteroid nuclear receptor b	2024	1892-1893AG>AG	S

M10901	M10901	138040	GEN-2W	Corticosteroid nuclear receptor b	2024	1892-1893delAG	F
M10901	M10901	138040	GEN-2W	Corticosteroid nuclear receptor b	2054	1922A>T	D641V
M10901	M10901	138040	GEN-2W	Corticosteroid nuclear receptor b	2372	2240T>G	I747S
M10901	M10901	138040	GEN-2W	Corticosteroid nuclear receptor b	2391	2259A>C	L753F
M10901	M10901	138040	GEN-2W	Corticosteroid nuclear receptor b	2391	2259A>T	L753F
M11050	M11050	138040	GEN-7Y	Glucocorticoid receptor	2166	2034C>T	S
M11050	M11050	138040	GEN-7Y	Glucocorticoid receptor	3353	3221T>G	3
M11050	M11050	138040	GEN-7Y	Glucocorticoid receptor	3398	3266T>G	3
M14565	M14565	118485	GEN-30	Cytochrome P450, subfamily XIA (cholesterol side chain cleavage)	947	903G>C	M301I
M14758	M14758	171050	GEN-1S6	P glycoprotein 1	978	554-555TT>GA>G	V185G
M14758	M14758	171050	GEN-1S6	P glycoprotein 1	978	554-555TT>TT	S
M14758	M14758	171050	GEN-1S6	P glycoprotein 1	1623	1199G>A	S400N
M14758	M14758	171050	GEN-1S6	P glycoprotein 1	3101	2677G>A	A893T
M14758	M14758	171050	GEN-1S6	P glycoprotein 1	3101	2677G>T	A893S
M14758	M14758	171050	GEN-1S6	P glycoprotein 1	3859	3435C>T	S
M14758	M14758	171050	GEN-1S6	P glycoprotein 1	4460	4036A>G	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	136	(-39)T>C	5
M15856	M15856	238600	GEN-33	Lipoprotein lipase	280	106G>A	D36N
M15856	M15856	238600	GEN-33	Lipoprotein lipase	438	264T>A	F
M15856	M15856	238600	GEN-33	Lipoprotein lipase	447	273G>A	F
M15856	M15856	238600	GEN-33	Lipoprotein lipase	474	300C>A	F
M15856	M15856	238600	GEN-33	Lipoprotein lipase	480	306A>C	R102S
M15856	M15856	238600	GEN-33	Lipoprotein lipase	511	337T>C	W113R
M15856	M15856	238600	GEN-33	Lipoprotein lipase	571	397C>T	F

M15856	M15856	238600	GEN-33	Lipoprotein lipase	680	506G>A	G169E
M15856	M15856	238600	GEN-33	Lipoprotein lipase	722	548A>G	D183G
M15856	M15856	238600	GEN-33	Lipoprotein lipase	770	596C>G	S199C
M15856	M15856	238600	GEN-33	Lipoprotein lipase	781	607G>A	A203T
M15856	M15856	238600	GEN-33	Lipoprotein lipase	795	621C>G	D207E
M15856	M15856	238600	GEN-33	Lipoprotein lipase	818	644G>A	G215E
M15856	M15856	238600	GEN-33	Lipoprotein lipase	836	662T>C	I221T
M15856	M15856	238600	GEN-33	Lipoprotein lipase	839	665G>A	G222E
M15856	M15856	238600	GEN-33	Lipoprotein lipase	867	693C>G	D231E
M15856	M15856	238600	GEN-33	Lipoprotein lipase	875	701C>T	P234L
M15856	M15856	238600	GEN-33	Lipoprotein lipase	916	742delG	F
M15856	M15856	238600	GEN-33	Lipoprotein lipase	983	809G>A	R270H
M15856	M15856	238600	GEN-33	Lipoprotein lipase	985	811T>A	S271T
M15856	M15856	238600	GEN-33	Lipoprotein lipase	1003	829G>A	D277N
M15856	M15856	238600	GEN-33	Lipoprotein lipase	1127	953A>G	N318S
M15856	M15856	238600	GEN-33	Lipoprotein lipase	1255	1081G>A	A361T
M15856	M15856	238600	GEN-33	Lipoprotein lipase	1348	1174C>G	L392V
M15856	M15856	238600	GEN-33	Lipoprotein lipase	1401	1227G>A	F
M15856	M15856	238600	GEN-33	Lipoprotein lipase	1508	1334G>A	C445Y
M15856	M15856	238600	GEN-33	Lipoprotein lipase	1595	1421C>G	F
M15856	M15856	238600	GEN-33	Lipoprotein lipase	1973	1799T>C	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	2428	2254T>A	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	2743	2569T>C	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	2851	2677A>G	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	2851	2677A>G	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	2958	2784G>A	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	3017	2843T>C	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	3272	3098T>C	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	3272	3098T>C	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	3343	3169T>C	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	3447	3273C>T	3
M15872	M15872	138360	GEN-QS	Human glutathione S-transferase 2 (GST) mRNA, complete cds	16	(-40)G>A	5
M15872	M15872	138360	GEN-QS	Human glutathione S-transferase 2 (GST) mRNA, complete cds	54	(-2)T>C	5

M15872	M15872	138360	GEN-QS	mRNA, complete cds	84	29T>C	F10S
				Human glutathione S-transferase 2 (GST)			
M15872	M15872	138360	GEN-QS	mRNA, complete cds	111	56C>T	T19I
				Human glutathione S-transferase 2 (GST)			
M15872	M15872	138360	GEN-QS	mRNA, complete cds	170	115G>T	F
				Human glutathione S-transferase 2 (GST)			
M15872	M15872	138360	GEN-QS	mRNA, complete cds	321	266G>A	R89K
				Human glutathione S-transferase 2 (GST)			
M15872	M15872	138360	GEN-QS	mRNA, complete cds	376	321C>T	S
				Human glutathione S-transferase 2 (GST)			
M15872	M15872	138360	GEN-QS	mRNA, complete cds	430	375G>A	S
				Human glutathione S-transferase 2 (GST)			
M15872	M15872	138360	GEN-QS	mRNA, complete cds	622	567C>T	S
				Human glutathione S-transferase 2 (GST)			
M15872	M15872	138360	GEN-QS	mRNA, complete cds	684	629A>C	E210A
				Human glutathione S-transferase 2 (GST)			
M15872	M15872	138360	GEN-QS	mRNA, complete cds	701	646G>T	A216S
				Human glutathione S-transferase 2 (GST)			
M16505	M16505	308100	GEN-7D	mRNA, complete cds	2725	2505T>G	3
				STERYL-SULFATASE			
M16505	M16505	308100	GEN-7D	PRECURSOR	4364	4144G>A	3
				STERYL-SULFATASE			
M16505	M16505	308100	GEN-7D	PRECURSOR	4665	4445A>G	3
				STERYL-SULFATASE			
M16505	M16505	308100	GEN-7D	PRECURSOR	5894	5674A>G	3
				STERYL-SULFATASE			
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	422	293A>G	D98G
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	557	428G>A	G143D
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	564	435-436TT>AG>A	F146V
						G	

M16541	M16541	177400	GEN-35	Butyrylcholinesterase	568	439C>T	F
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	596	467A>G	Y156C
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	941	812C>T	T271M
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	961	832A>C	T278P
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	978	849G>C	E283D
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1201	1072T>A	L358I
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1306	1177G>A	G393R
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1382	1253G>T	G418V
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1549	1420T>G	F474V
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1564	1435G>T	F
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1703	1574A>T	E525V
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1756	1627C>T	R543C
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1828	1699G>A	A567T
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1828	1699G>A	A567T
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	2127	1998A>G	3
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	2127	1998A>G	3
M16827	M16827	201450	GEN-EI	Acyl-Coenzyme A dehydrogenase, C-4 to C- 12 straight chain	1956	1938T>C	3
M20681	M20681	138170	GEN- 230	Human glucose transporter-like protein-III (GLUT3), complete cds	1550	1308C>T	S
M20681	M20681	138170	GEN- 230	Human glucose transporter-like protein-III (GLUT3), complete cds	3179	2937T>C	3
M20681	M20681	138170	GEN- 230	Human glucose transporter-like protein-III (GLUT3), complete cds	3238	2996C>T	3
M20681	M20681	138170	GEN- 230	Human glucose transporter-like protein-III (GLUT3), complete cds	3356	3114T>C	3
M20681	M20681	138170	GEN- 230	Human glucose transporter-like protein-III (GLUT3), complete cds	3378	3136T>C	3
M20681	M20681	138170	GEN- 230	Human glucose transporter-like protein-III (GLUT3), complete cds	3524	3282C>A	3
M20681	M20681	138170	GEN- 230	Human glucose transporter-like protein-III (GLUT3), complete cds	3572	3330G>T	3

M21054	M21054	172410	GEN-3B	(GLUT3), complete cds Phospholipase A-2 (PLA-2) lung	331	294G>A	S
M21054	M21054	172410	GEN-3B	Phospholipase A-2 (PLA-2) lung	400	363C>A	D121E
M24400	M24400	118890	GEN-R2	Human chymotrypsinogen mRNA, complete cds	121	105G>A	S
M24400	M24400	118890	GEN-R2	Human chymotrypsinogen mRNA, complete cds	231	215C>A	T72N
M24400	M24400	118890	GEN-R2	Human chymotrypsinogen mRNA, complete cds	460	444C>T	S
M24400	M24400	118890	GEN-R2	Human chymotrypsinogen mRNA, complete cds	649	633C>T	S
M24857	M24857	180190	GEN-80	Human chymotrypsinogen mRNA, complete cds Retinoic acid receptor, gamma 1	1694	1280C>T	S427L
M24895	M24895	104660	GEN-R3	Homo sapiens alpha- amylase mRNA, complete cds	193	147C>G	S
M24895	M24895	104660	GEN-R3	Homo sapiens alpha- amylase mRNA, complete cds	967	921A>G	S
M24895	M24895	104660	GEN-R3	Homo sapiens alpha- amylase mRNA, complete cds	1009	963G>C	S
M24895	M24895	104660	GEN-R3	Homo sapiens alpha- amylase mRNA, complete cds	1027	981T>A	S
M24895	M24895	104660	GEN-R3	Homo sapiens alpha- amylase mRNA, complete cds	1054	1008T>C	S
M24895	M24895	104660	GEN-R3	Homo sapiens alpha- amylase mRNA, complete cds	1093	1047T>A	S
M24895	M24895	104660	GEN-R3	Homo sapiens alpha- amylase mRNA, complete cds	1178	1132A>G	N378D
M24895	M24895	104660	GEN-R3	Homo sapiens alpha- amylase mRNA, complete cds	1191	1145T>C	I382T
M24895	M24895	104660	GEN-R3	Homo sapiens alpha- amylase mRNA, complete cds	1394	1348A>T	T450S

M24895	M24895	104660	GEN-R3	cds Homo sapiens alpha-amylase mRNA, complete	1474	1428T>C	S
M24895	M24895	104660	GEN-R3	cds Homo sapiens alpha-amylase mRNA, complete	1492	1446C>T	S
M24895	M24895	104660	GEN-R3	cds Homo sapiens alpha-amylase mRNA, complete	1504	1458C>T	S
M24895	M24895	104660	GEN-R3	cds Homo sapiens alpha-amylase mRNA, complete	1543	1497G>A	S
M24895	M24895	104660	GEN-R3	cds Homo sapiens alpha-amylase mRNA, complete	1579	1533A>G	S
M24895	M24895	104660	GEN-R3	cds Homo sapiens alpha-amylase mRNA, complete	1601	1555T>A	3
M26393	M26393	201470	GEN-EW	Acyl-Coenzyme A dehydrogenase, C-2 to C-3 short chain subfamily IIB	1797	1765A>G	3
M29874	M29874	None	GEN-3I	Cytochrome P450, subfamily IIB (phenobarbital-inducible), polypeptide 6	2758	2752T>A	3
M29874	M29874	None	GEN-3I	Cytochrome P450, subfamily IIB (phenobarbital-inducible), polypeptide 6	2836	2830G>A	3
M29874	M29874	None	GEN-3I	Cytochrome P450, subfamily IIB (phenobarbital-inducible), polypeptide 6	2902	2896T>C	3
M29882	M29882	107670	GEN-6R	Apolipoprotein A-II	26	17C>A	A6E
M29882	M29882	107670	GEN-6R	Apolipoprotein A-II	183	174G>A	S
M29882	M29882	107670	GEN-6R	Apolipoprotein A-II	192	183C>A	S
M34479	M34479	179060	GEN-F9	Pyruvate dehydrogenase (lipoamide) beta	109	109G>A	D37N
M34479	M34479	179060	GEN-F9	Pyruvate dehydrogenase (lipoamide) beta	438	438A>G	S

M34479	M34479	179060	GEN-F9	Pyruvate dehydrogenase (lipoamide) beta	1172	1172A>C	3
M34479	M34479	179060	GEN-F9	Pyruvate dehydrogenase (lipoamide) beta	1179	1179C>T	3
M34479	M34479	179060	GEN-F9	Pyruvate dehydrogenase (lipoamide) beta	1323	1323C>A	3
M34479	M34479	179060	GEN-F9	Pyruvate dehydrogenase (lipoamide) beta	1376	1376G>C	3
M34479	M34479	179060	GEN-F9	Pyruvate dehydrogenase (lipoamide) beta	1433	1433C>T	3
M55040	M55040	100740	GEN-3Q	acetylcholinesterase	323	167C>T	P56L
M55040	M55040	100740	GEN-3Q	acetylcholinesterase	1154	998T>A	V333E
M55040	M55040	100740	GEN-3Q	acetylcholinesterase	1213	1057C>A	H353N
M55040	M55040	100740	GEN-3Q	acetylcholinesterase	1482	1326G>T	S
M55040	M55040	100740	GEN-3Q	acetylcholinesterase	1587	1431C>T	S
M55040	M55040	100740	GEN-3Q	acetylcholinesterase	1587	1431C>T	S
M55040	M55040	100740	GEN-3Q	acetylcholinesterase	1663	1507T>C	F503L
M55531	M55531	138230	GEN-FF	Solute carrier family 2 (facilitated glucose transporter), member 5	1208	1133T>G	V378G
M55531	M55531	138230	GEN-FF	Solute carrier family 2 (facilitated glucose transporter), member 5	1975	1900C>T	3
M55531	M55531	138230	GEN-FF	Solute carrier family 2 (facilitated glucose transporter), member 5	1985	1910A>G	3
M57899	M57899	191740	GEN-38A	Human bilirubin UDP-glucuronosyltransferase isozyme 1 mRNA, complete cds	1828	1813C>T	3
M57899	M57899	191740	GEN-38A	Human bilirubin UDP-glucuronosyltransferase isozyme 1 mRNA, complete cds	1956	1941C>G	3
M57899	M57899	191740	GEN-38A	Human bilirubin UDP-glucuronosyltransferase isozyme 1 mRNA, complete cds	2057	2042C>G	3
M58525	M58525	116790	GEN-3S	Catechol-O-methyltransferase	390	186T>C	S

M58525	M58525	116790	GEN-3S	Catechol-O-methyltransferase	390	186T>C	S
M58525	M58525	116790	GEN-3S	Catechol-O-methyltransferase	418	214G>T	A72S
M58525	M58525	116790	GEN-3S	Catechol-O-methyltransferase	423	219G>A	S
M58525	M58525	116790	GEN-3S	Catechol-O-methyltransferase	612	408C>G	S
M58525	M58525	116790	GEN-3S	Catechol-O-methyltransferase	676	472A>G	M158V
M58525	M58525	116790	GEN-3S	Catechol-O-methyltransferase	676	472A>G	M158V
M58525	M58525	116790	GEN-3S	Catechol-O-methyltransferase	813	609C>T	S
M58525	M58525	116790	GEN-3S	Catechol-O-methyltransferase	1031	827delC	F
M58525	M58525	116790	GEN-3S	Catechol-O-methyltransferase	1039	835C>A	3
M60761	M60761	156569	GEN-FL	O-6-methylguanine-DNA methyltransferase	174	159C>T	S
M60761	M60761	156569	GEN-FL	O-6-methylguanine-DNA methyltransferase	174	159C>T	S
M60761	M60761	156569	GEN-FL	O-6-methylguanine-DNA methyltransferase	174	159C>T	S
M60761	M60761	156569	GEN-FL	O-6-methylguanine-DNA methyltransferase	210	195G>C	W65C
M60761	M60761	156569	GEN-FL	O-6-methylguanine-DNA methyltransferase	264	249A>T	S
M60761	M60761	156569	GEN-FL	O-6-methylguanine-DNA methyltransferase	265	250C>T	L84F
M60761	M60761	156569	GEN-FL	O-6-methylguanine-DNA methyltransferase	265	250C>T	L84F
M60761	M60761	156569	GEN-FL	O-6-methylguanine-DNA methyltransferase	442	427A>G	I143V
M60761	M60761	156569	GEN-FL	O-6-methylguanine-DNA methyltransferase	442	427A>G	I143V
M60761	M60761	156569	GEN-FL	O-6-methylguanine-DNA methyltransferase	493	478G>A	G160R
M60761	M60761	156569	GEN-FL	O-6-methylguanine-DNA methyltransferase	548	533A>G	K178R
M60761	M60761	156569	GEN-FL	O-6-methylguanine-DNA methyltransferase	582	567G>A	S

M61855	M61855	601130	GEN-3C1	methytransferase Human cytochrome P450C9 (CYP2C9) mRNA, clone 25	852	853T>A	3
M61855	M61855	601130	GEN-3C1	Human cytochrome P450C9 (CYP2C9) mRNA, clone 25	1085	1086A>G	3
M61855	M61855	601130	GEN-3C1	Human cytochrome P450C9 (CYP2C9) mRNA, clone 25	1437	1438T>A	3
M63012	M63012	168820	GEN-9F	Paraoxonase 1	172	163A>T	M55L
M63509	M63509	138380	GEN-9G	Glutathione S-transferase M2 (muscle)	644	628A>T	T210S
M64082	M64082	136130	GEN-9H	Flavin-containing monooxygenase 1 (DIMETHYLANILINE MONOOXYGENASE)	1286	1188A>G	S
M64082	M64082	136130	GEN-9H	Flavin-containing monooxygenase 1 (DIMETHYLANILINE MONOOXYGENASE)	1808	1710C>T	3
M64082	M64082	136130	GEN-9H	Flavin-containing monooxygenase 1 (DIMETHYLANILINE MONOOXYGENASE)	1904	1806C>T	3
M64592	M64592	120420	GEN-3X	Granulocyte colony- stimulating factor	271	271T>G	Y91D
M64592	M64592	120420	GEN-3X	Granulocyte colony- stimulating factor	1533	1533C>T	S
M64799	M64799	None	GEN-4DN	Histamine receptor H2	398	398T>C	V133A
M64799	M64799	None	GEN-4DN	Histamine receptor H2	525	525A>T	K175N
M64799	M64799	None	GEN-4DN	Histamine receptor H2	620	620A>G	K207R
M64799	M64799	None	GEN-4DN	Histamine receptor H2	649	649A>G	N217D
M64799	M64799	None	GEN-4DN	Histamine receptor H2	692	692A>G	K231R
M64799	M64799	None	GEN-4DN	Histamine receptor H2	802	802G>A	V268M

M68867	M68867	180231	GEN-S1	Human cellular retinoic acid-binding protein II (CRABP) mRNA, complete cds	604	506C>A	3
M68895	M68895	103735	GEN-MH7	Human alcohol dehydrogenase 6 gene, complete cds	547	454G>A	V152M
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	435	385A>C	S
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	936	886C>T	F
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	941	891T>G	S
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	941	891T>G	S
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	1076	1026A>T	S
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	1373	1323G>A	F
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	1460	1410C>T	S
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	1460	1410C>T	S
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	1609	1559A>G	K520R
M80244	M80244	600182	GEN-3UJ	Human E16 mRNA, complete cds	202	(-109)G>C	5
M80244	M80244	600182	GEN-3UJ	Human E16 mRNA, complete cds	520	210T>C	S
M80244	M80244	600182	GEN-3UJ	Human E16 mRNA, complete cds	1185	875G>A	3
M80244	M80244	600182	GEN-3UJ	Human E16 mRNA, complete cds	1473	1163C>G	3
M80244	M80244	600182	GEN-3UJ	Human E16 mRNA, complete cds	1692	1382C>T	3
M80244	M80244	600182	GEN-3UJ	Human E16 mRNA, complete cds	2591	2281A>G	3
M80244	M80244	600182	GEN-3UJ	Human E16 mRNA, complete cds	3138	2828G>C	3
M80244	M80244	600182	GEN-3UJ	Human E16 mRNA, complete cds	3538	3228T>C	3
M96234	M96234	138333	GEN-9J	Glutathione S-transferase M4	797	534T>C	S
M98045	M98045	136510	GEN-4C3	Homo sapiens folypolyglutamate synthetase mRNA, complete cds	802	732C>T	S
M98045	M98045	136510	GEN-4C3	Homo sapiens folypolyglutamate	1747	1677G>T	3

M98045	M98045	136510	GEN-4C3	synthetase mRNA, complete cds Homo sapiens folypolyglutamate synthetase mRNA, complete cds	1900	1830T>C	3
M98045	M98045	136510	GEN-4C3	synthetase mRNA, complete cds Homo sapiens folypolyglutamate synthetase mRNA, complete cds	1900	1830T>C	3
M98045	M98045	136510	GEN-4C3	synthetase mRNA, complete cds Homo sapiens folypolyglutamate synthetase mRNA, complete cds	1912	1842G>A	3
M98045	M98045	136510	GEN-4C3	synthetase mRNA, complete cds Homo sapiens folypolyglutamate synthetase mRNA, complete cds	1995	1925C>G	3
MDCR	L13385	601545	GEN-106	synthetase mRNA, complete cds Homo sapiens(clone 71) Miller-Dieker lissencephaly protein (LIS1) mRNA, complete cds	1467	1250C>T	3
MDCR	L13385	601545	GEN-106	synthetase mRNA, complete cds Homo sapiens(clone 71) Miller-Dieker lissencephaly protein (LIS1) mRNA, complete cds	1868	1651C>T	3
MDCR	L13385	601545	GEN-106	synthetase mRNA, complete cds Homo sapiens(clone 71) Miller-Dieker lissencephaly protein (LIS1) mRNA, complete cds	1917	1700C>T	3
MDCR	L13385	601545	GEN-106	synthetase mRNA, complete cds Homo sapiens(clone 71) Miller-Dieker lissencephaly protein (LIS1) mRNA, complete cds	2962	2745G>T	3
MDCR	L13385	601545	GEN-106	synthetase mRNA, complete cds Homo sapiens(clone 71) Miller-Dieker lissencephaly protein (LIS1) mRNA, complete cds	4589	4372G>A	3
MTP	X75500	157147	GEN-307	synthetase mRNA, complete cds H.sapiens mRNA for microsomal triglyceride transfer protein	1847	1823T>G	F608C

MTP	X75500	157147	GEN-307	H.sapiens mRNA for microsomal triglyceride transfer protein Human, NAD(P)H:menadione oxidoreductase mRNA, complete cds	3231	3207G>A	3
NMOR1	J03934	125860	GEN-12L	Human, NAD(P)H:menadione oxidoreductase mRNA, complete cds	609	559C>T	P187S
NMOR1	J03934	125860	GEN-12L	Human, NAD(P)H:menadione oxidoreductase mRNA, complete cds	1784	1734T>G	3
NMOR1	J03934	125860	GEN-12L	Human, NAD(P)H:menadione oxidoreductase mRNA, complete cds	1994	1944C>T	3
NMOR2	J02888	160998	GEN-XT	Human quinone oxidoreductase (NQO2) mRNA, complete cds	505	330G>A	S
NMOR2	J02888	160998	GEN-XT	Human quinone oxidoreductase (NQO2) mRNA, complete cds	909	734G>C	3
NRAMP1	L32185	600266	GEN-21Y	Homo sapiens integral membrane protein (NRAMP1) mRNA, complete cds	1399	1323C>T	S
NRAMP2	L37347	600523	GEN-206	Human integral membrane protein (Nramp2) mRNA, partial	1092	1083C>T	S
ORM1	M13692	138600	GEN-1P5	Human alpha-1 acid glycoprotein mRNA, complete cds	128	113A>G	Q38R
ORM1	M13692	138600	GEN-1P5	Human alpha-1 acid glycoprotein mRNA, complete cds	222	207C>T	S
ORM1	M13692	138600	GEN-1P5	Human alpha-1 acid glycoprotein mRNA, complete cds	273	258A>C	S
ORM1	M13692	138600	GEN-1P5	Human alpha-1 acid glycoprotein mRNA, complete cds	296	281C>A	T94N
ORM1	M13692	138600	GEN-1P5	Human alpha-1 acid glycoprotein mRNA, complete cds	514	499C>T	R167C

ORM1	M13692	138600	1P5	glycoprotein mRNA, complete cds	535	520G>A	V174M
ORM1	M13692	138600	GEN-1P5	Human alpha-1 acid glycoprotein mRNA, complete cds	654	639G>T	3
PDHA1	X52709	312170	GEN-33Y	Human alpha-1 acid glycoprotein mRNA, complete cds	849	795A>G	S
PDHA1	X52709	312170	GEN-33Y	Human mRNA for brain pyruvate dehydrogenase (EC 1.2.4.1)	1337	1283C>T	3
PDHA1	X52709	312170	GEN-33Y	Human mRNA for brain pyruvate dehydrogenase (EC 1.2.4.1)	1416	1362G>A	3
PLA2G2A	M22430	172411	GEN-25V	Human RASF-A PLA2 mRNA, complete cds	116	(-20)G>T	5
PLA2G2A	M22430	172411	GEN-25V	Human RASF-A PLA2 mRNA, complete cds	231	96G>C	S
PLA2G2A	M22430	172411	GEN-25V	Human RASF-A PLA2 mRNA, complete cds	267	132C>T	S
PLA2G2A	M22430	172411	GEN-25V	Human RASF-A PLA2 mRNA, complete cds	267	132C>T	S
PLA2G2A	M22430	172411	GEN-25V	Human RASF-A PLA2 mRNA, complete cds	278	143-144GT>GT	S
PLA2G2A	M22430	172411	GEN-25V	Human RASF-A PLA2 mRNA, complete cds	278	143-144delGT	F
PLA2G2A	M22430	172411	GEN-25V	Human RASF-A PLA2 mRNA, complete cds	643	508C>T	3
PLA2G2A	M22430	172411	GEN-25V	Human RASF-A PLA2 mRNA, complete cds	700	565G>C	3
PNLIP	M93285	246600	GEN-48N	Pancreatic lipase (PNLIP) (Dietary supplement)	646	646G>T	V216L
PRSS1	M22612	276000	GEN-26A	Human pancreatic trypsin 1 (TRY1) mRNA, complete cds	34	28G>T	V10L
PRSS1	M22612	276000	GEN-26A	Human pancreatic trypsin 1 (TRY1) mRNA, complete cds	61	55G>A	D19N

PRSS1	M22612	276000	GEN-26A	Human pancreatic trypsin 1 (TRY1) mRNA, complete cds	97	91G>A	E31K
PRSS1	M22612	276000	GEN-26A	Human pancreatic trypsin 1 (TRY1) mRNA, complete cds	198	192C>T	S
PRSS1	M22612	276000	GEN-26A	Human pancreatic trypsin 1 (TRY1) mRNA, complete cds	412	406G>T	G136C
PRSS1	M22612	276000	GEN-26A	Human pancreatic trypsin 1 (TRY1) mRNA, complete cds	492	486T>C	S
PRSS1	M22612	276000	GEN-26A	Human pancreatic trypsin 1 (TRY1) mRNA, complete cds	711	705C>T	S
PRSS1	M22612	276000	GEN-26A	Human pancreatic trypsin 1 (TRY1) mRNA, complete cds	744	738T>C	S
PRSS2	M27602	601564	GEN-2C7	Human pancreatic trypsinogen (TRY2) mRNA, complete cds	29	23C>T	T8I
PRSS2	M27602	601564	GEN-2C7	Human pancreatic trypsinogen (TRY2) mRNA, complete cds	34	28G>T	V10F
PRSS2	M27602	601564	GEN-2C7	Human pancreatic trypsinogen (TRY2) mRNA, complete cds	61	55G>A	D19N
PRSS2	M27602	601564	GEN-2C7	Human pancreatic trypsinogen (TRY2) mRNA, complete cds	97	91G>A	E31K
PRSS2	M27602	601564	GEN-2C7	Human pancreatic trypsinogen (TRY2) mRNA, complete cds	198	192C>T	S
PRSS2	M27602	601564	GEN-2C7	Human pancreatic trypsinogen (TRY2) mRNA, complete cds	276	270G>A	S
PXMP1	X58528	170995	GEN-392	Human PMP70 mRNA for a peroxisomal membrane protein	2375	2351C>T	3
SLC18A3	U09210	600336	GEN-4F3	Human vesicular acetylcholine transporter	1369	927A>G	S

SLC18A3	U09210	600336	GEN-4F3	mRNA, complete cds Human vesicular acetylcholine transporter	1567	1125C>G	S
SLC18A3	U09210	600336	GEN-4F3	mRNA, complete cds Human vesicular acetylcholine transporter	2080	1638G>T	3
SLC18A3	U09210	600336	GEN-4F3	mRNA, complete cds Human vesicular acetylcholine transporter	2199	1757G>A	3
SLC18A3	U09210	600336	GEN-4F3	mRNA, complete cds Human vesicular acetylcholine transporter	2349	1907G>T	3
SLC5A1	M24847	182380	GEN-28S	mRNA, complete cds Human Na ⁺ /glucose cotransporter 1 mRNA,	2226	2216C>T	3
SLC6A3	L24178	126455	GEN-28S	complete cds Homo sapiens dopamine transporter mRNA,	1917	1898C>T	3
SOAT	L21934	102642	GEN-25C	complete cds Human acyl coenzyme A:cholesterol acyltransferase mRNA,	676	(-721)T>G	5
SOAT	L21934	102642	GEN-25C	complete cds Human acyl coenzyme A:cholesterol acyltransferase mRNA,	814	(-583)C>T	5
SOAT	L21934	102642	GEN-25C	complete cds Human acyl coenzyme A:cholesterol acyltransferase mRNA,	1993	597C>T	S
SOAT	L21934	102642	GEN-25C	complete cds Human acyl coenzyme A:cholesterol acyltransferase mRNA,	2365	969C>T	S
SOAT	L21934	102642	GEN-25C	complete cds Human acyl coenzyme A:cholesterol acyltransferase mRNA,	2821	1425G>C	S
SOAT	L21934	102642	GEN-25C	complete cds Human acyl coenzyme A:cholesterol acyltransferase mRNA,	3537	2141T>C	3

SOD2	X07834	147460	GEN-1ES	acyltransferase mRNA, complete cds	44	40C>G	P14A
SOD2	X07834	147460	GEN-1ES	Human mRNA for manganese superoxide dismutase (EC 1.15.1.1)	51	47T>C	V16A
SOD2	X07834	147460	GEN-1ES	Human mRNA for manganese superoxide dismutase (EC 1.15.1.1)	198	194C>A	T65N
SOD2	X07834	147460	GEN-1ES	Human mRNA for manganese superoxide dismutase (EC 1.15.1.1)	249	245T>C	I82T
SOD3	J02947	185490	GEN-Y3	Human extracellular-superoxide dismutase (SOD3) mRNA, complete cds	1042	973C>T	3
SPINK1	Y00705	167790	GEN-UA	Homo sapiens pstl mRNA for pancreatic secretory inhibitor (expressed in neoplastic tissue)	332	272C>T	3
TAP2	Z22935	170261	GEN-26P	H.sapiens TAP2B mRNA, complete CDS	1163	1135G>A	V379I
TAP2	Z22935	170261	GEN-26P	H.sapiens TAP2B mRNA, complete CDS	1186	1158G>T	S
TAP2	Z22935	170261	GEN-26P	H.sapiens TAP2B mRNA, complete CDS	1840	1812G>A	S
TAP2	Z22935	170261	GEN-26P	H.sapiens TAP2B mRNA, complete CDS	2021	1993G>A	A665T
TAP2	Z22935	170261	GEN-26P	H.sapiens TAP2B mRNA, complete CDS	2087	2059C>T	F
TAP2	Z22935	170261	GEN-26P	H.sapiens TAP2B mRNA, complete CDS	2119	2091T>G	S
TBG	M14091	314200	GEN-1QO	Human thyroxine-binding globulin mRNA, complete cds	901	571G>A	D191N
TBG	M14091	314200	GEN-1QO	Human thyroxine-binding globulin mRNA, complete cds	1239	909G>T	L303F
TCN2	M60396	275350	GEN-	Human transcobalamin II	1164	1127C>T	S376L

TCN2	3AX	M60396	275350	3AX	(TCII) mRNA, complete cds	1765	1728T>C	3
TPMT	GEN-1LY	U12387	187680	GEN-1LY	Human thiopurine methyltransferase (TPMT) mRNA, complete cds	536	460G>A	A154T
TPMT	GEN-1LY	U12387	187680	GEN-1LY	Human thiopurine methyltransferase (TPMT) mRNA, complete cds	795	719A>G	Y240C
TPMT	GEN-1LY	U12387	187680	GEN-1LY	Human thiopurine methyltransferase (TPMT) mRNA, complete cds	1085	1009T>C	3
TPMT	GEN-1LY	U12387	187680	GEN-1LY	Human thiopurine methyltransferase (TPMT) mRNA, complete cds	1336	1260C>T	3
TPMT	GEN-1LY	U12387	187680	GEN-1LY	Human thiopurine methyltransferase (TPMT) mRNA, complete cds	1373	1297G>A	3
TPP2	GEN-35U	M55169	190470	GEN-35U	Homo sapiens tripeptidyl peptidase II mRNA, 3 end	2681	2681T>G	F894C
TPP2	GEN-35U	M55169	190470	GEN-35U	Homo sapiens tripeptidyl peptidase II mRNA, 3 end	3637	3637G>A	3
U03858	GEN-MDM	U03858	600007	GEN-MDM	Fms-related tyrosine kinase 3 ligand	683	600C>T	S
U03858	GEN-MDM	U03858	600007	GEN-MDM	Fms-related tyrosine kinase 3 ligand	1016	933T>C	3
U06088	GEN-MP3	U06088	253000	GEN-MP3	Human N-acetylgalactosamine 6-sulphatase (GALNS) gene	1936	1936C>T	3
U06088	GEN-MP3	U06088	253000	GEN-MP3	Human N-acetylgalactosamine 6-sulphatase (GALNS) gene	2180	2180G>A	3
U06088	GEN-MP3	U06088	253000	GEN-MP3	Human N-acetylgalactosamine 6-sulphatase (GALNS) gene	2221	2221G>A	3
U07132	GEN-7M	U07132	600380	GEN-7M	Orphan receptor	763	519G>A	S
U07132	GEN-7M	U07132	600380	GEN-7M	Orphan receptor	1399	1155C>T	S
U07132	GEN-7M	U07132	600380	GEN-7M	Orphan receptor	1726	1482G>C	3
U07132	GEN-7M	U07132	600380	GEN-7M	Orphan receptor	1952	1708C>G	3

U08021	U08021	600008	GEN-1FG	Human nicotinamide N-methyltransferase (NNMT) mRNA, complete cds	584	467C>G	P156R
U08021	U08021	600008	GEN-1FG	Human nicotinamide N-methyltransferase (NNMT) mRNA, complete cds	613	496C>T	S
U08989	U08989	133550	GEN-CBZ	Human glutamate transporter mRNA, complete cds	684	519C>T	S
U08989	U08989	133550	GEN-CBZ	Human glutamate transporter mRNA, complete cds	1617	1452T>C	S
U09178	U09178	274270	GEN-HA	Dihydropyrimidine Dehydrogenase	166	85T>C	C29R
U09178	U09178	274270	GEN-HA	Dihydropyrimidine Dehydrogenase	166	85T>C	C29R
U09178	U09178	274270	GEN-HA	Dihydropyrimidine Dehydrogenase	577	496A>G	M166V
U09178	U09178	274270	GEN-HA	Dihydropyrimidine Dehydrogenase	638	557A>G	Y186C
U09178	U09178	274270	GEN-HA	Dihydropyrimidine Dehydrogenase	1708	1627A>G	I543V
U09178	U09178	274270	GEN-HA	Dihydropyrimidine Dehydrogenase	3432	3351T>C	3
U09178	U09178	274270	GEN-HA	Dihydropyrimidine Dehydrogenase	3730	3649G>A	3
U09178	U09178	274270	GEN-HA	Dihydropyrimidine Dehydrogenase	3925	3844A>G	3
U09178	U09178	274270	GEN-HA	Dihydropyrimidine Dehydrogenase	3937	3856T>C	3
U10868	U10868	600466	GEN-1JF	Human aldehyde dehydrogenase ALDH7 mRNA, complete cds	2681	2634T>C	3
U16660	U16660	600696	GEN-1YD	Human peroxisomal enoyl-CoA hydratase-like protein (HPXEL) mRNA, complete cds	149	122A>C	E41A
U16660	U16660	600696	GEN-1YD	Human peroxisomal enoyl-CoA hydratase-like protein (HPXEL) mRNA, complete cds	402	375G>A	S

U16660	U16660	600696	GEN-1YD	Human peroxisomal enoyl-CoA hydratase-like protein (HPXEL) mRNA, complete cds	802	775C>G	P259A
U16660	U16660	600696	GEN-1YD	Human peroxisomal enoyl-CoA hydratase-like protein (HPXEL) mRNA, complete cds	1157	1130G>A	3
U17986	U17986	300036	GEN-20X	Human GABA/noradrenaline transporter mRNA, complete cds	1161	1132G>A	V378M
U17986	U17986	300036	GEN-20X	Human GABA/noradrenaline transporter mRNA, complete cds	1670	1641C>T	S
U17986	U17986	300036	GEN-20X	Human GABA/noradrenaline transporter mRNA, complete cds	2034	2005G>A	V669M
U17986	U17986	300036	GEN-20X	Human GABA/noradrenaline transporter mRNA, complete cds	2088	2059C>T	R687C
U17986	U17986	300036	GEN-20X	Human GABA/noradrenaline transporter mRNA, complete cds	2150	2121C>T	S
U17986	U17986	300036	GEN-20X	Human GABA/noradrenaline transporter mRNA, complete cds	2231	2202A>G	3
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	53	(-43)T>C	5
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	175	80G>A	R27H
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	175	80G>A	R27H
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	341	246C>G	S
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	791	696C>T	S

U19720	U19720	600424	GEN-11	(SLC19A1) Folate Transporter	1067	972G>A	S
U19720	U19720	600424	GEN-11	(SLC19A1) Folate Transporter	2100	2005*2006ins G	F
U19720	U19720	600424	GEN-11	(SLC19A1) Folate Transporter	2582	2487T>G	3
U19720	U19720	600424	GEN-11	(SLC19A1) Folate Transporter	2582	2487T>G	3
U19720	U19720	600424	GEN-11	(SLC19A1) Folate Transporter	2617	2522C>T	3
U19720	U19720	600424	GEN-11	(SLC19A1) Folate Transporter	2617	2522C>T	3
U19720	U19720	600424	GEN-11	(SLC19A1) Folate Transporter	2652	2557T>C	3
U19977	U19977	600688	GEN-22Q	Human preprocarboxypeptidase A2 (proCPA2) mRNA, complete cds	631	627C>T	S
U20157	U20157	601690	GEN-234	Human platelet-activating factor acetylhydrolase mRNA, complete cds	1297	1136T>C	V379A
U25029	U25029	138040	GEN-82	Glucocorticoid receptor alpha	335	335C>T	3
U25029	U25029	138040	GEN-82	Glucocorticoid receptor alpha	386	386T>C	3
U25029	U25029	138040	GEN-82	Glucocorticoid receptor alpha	1069	1069C>T	3
U27699	U27699	603080	GEN-2C9	Human pephBGT-1 betaine-GABA transporter mRNA, complete cds	2841	2255C>T	3
U34252	U34252	602733	GEN-3O5	Human gamma- aminobutyraldehyde dehydrogenase mRNA, complete cds	2417	2040G>A	3
U34252	U34252	602733	GEN-3O5	Human gamma- aminobutyraldehyde dehydrogenase mRNA, complete cds	2471	2094A>C	3
U34252	U34252	602733	GEN-3O5	Human gamma- aminobutyraldehyde dehydrogenase mRNA, complete cds	2674	2297A>C	3

U34252	U34252	602733	GEN-305	dehydrogenase mRNA, complete cds Human gamma-aminobutyraldehyde dehydrogenase mRNA, complete cds	2676	2299A>C	3
U35735	U35735	111000	GEN-2MN	Human RACH1 (RACH1) mRNA, complete cds	1006	838A>G	N280D
U35735	U35735	111000	GEN-2MN	Human RACH1 (RACH1) mRNA, complete cds	2619	2451T>C	3
U35735	U35735	111000	GEN-2MN	Human RACH1 (RACH1) mRNA, complete cds	2706	2538T>C	3
U36601	U36601	603268	GEN-IR	Heparan N-deacetylase/N-sulfotransferase-2	2727	2700T>G	3
U36601	U36601	603268	GEN-IR	Heparan N-deacetylase/N-sulfotransferase-2	2972	2945A>G	3
U37143	U37143	601258	GEN-2NS	Human cytochrome P450 monooxygenase CYP2J2 mRNA, complete cds	338	333G>C	S
U37143	U37143	601258	GEN-2NS	Human cytochrome P450 monooxygenase CYP2J2 mRNA, complete cds	1545	1540C>T	3
U53347	U53347	109190	GEN-34A	Human neutral amino acid transporter B mRNA, complete cds	2868	2249A>T	3
U55206	U55206	None	GEN-35Z	Homo sapiens human gamma-glutamyl hydrolase (hGH) mRNA, complete cds	75	16T>C	C6R
U55206	U55206	None	GEN-35Z	Homo sapiens human gamma-glutamyl hydrolase (hGH) mRNA, complete cds	150	91G>A	A31T
U55206	U55206	None	GEN-35Z	Homo sapiens human gamma-glutamyl hydrolase (hGH) mRNA, complete cds	511	452C>T	T151I
U55206	U55206	None	GEN-35Z	Homo sapiens human gamma-glutamyl hydrolase (hGH) mRNA, complete cds	1161	1102A>G	3

U70867	U70867	601460	GEN-4S	prostaglandin transporter hPGT	2706	2615T>G	3
U70867	U70867	601460	GEN-4S	prostaglandin transporter hPGT	2839	2748T>A	3
U70867	U70867	601460	GEN-4S	prostaglandin transporter hPGT	2908	2817A>G	3
U70867	U70867	601460	GEN-4S	prostaglandin transporter hPGT	3171	3080A>G	3
U70867	U70867	601460	GEN-4S	prostaglandin transporter hPGT	3171	3080A>G	3
U70867	U70867	601460	GEN-4S	prostaglandin transporter hPGT	3253	3162A>G	3
U70867	U70867	601460	GEN-4S	prostaglandin transporter hPGT	3255	3164A>G	3
U70867	U70867	601460	GEN-4S	prostaglandin transporter hPGT	3594	3503T>A	3
U79745	U79745	None	GEN- LPT	Homo sapiens monocarboxylate transporter homologue MCT6 mRNA, complete cds	2095	1930G>A	3
U81375	U81375	602193	GEN- 3VO	Human placental equilibrative nucleoside transporter 1 (hENT1) mRNA, complete cds	1989	1811G>A	3
U81375	U81375	602193	GEN- 3VO	Human placental equilibrative nucleoside transporter 1 (hENT1) mRNA, complete cds	1996	1818C>T	3
U81375	U81375	602193	GEN- 3VO	Human placental equilibrative nucleoside transporter 1 (hENT1) mRNA, complete cds	2045	1867T>C	3
U81800	U81800	None	GEN- 3WB	Homo sapiens monocarboxylate transporter (MCT3) mRNA, complete cds	1624	1562G>C	3
U92314	U92314	604125	GEN- 47U	Homo sapiens hydroxysteroid sulfotransferase SULT2B1a (HSST2)	1146	771C>T	S

U92314	U92314	604125	GEN-47U	mRNA, complete cds Homo sapiens hydroxysteroid sulfotransferase SULT2B1a (HSST2)	1164	789C>T	S
U92314	U92314	604125	GEN-47U	mRNA, complete cds Homo sapiens hydroxysteroid sulfotransferase SULT2B1a (HSST2)	1278	903T>C	S
V00494	V00494	103600	GEN-TL	mRNA, complete cds Human messenger RNA for serum albumin (HSA)	34	(-6)G>T	5
V00494	V00494	103600	GEN-TL	Human messenger RNA for serum albumin (HSA)	36	(-4)C>G	5
V00494	V00494	103600	GEN-TL	Human messenger RNA for serum albumin (HSA)	401	362G>A	G121E
V00494	V00494	103600	GEN-TL	Human messenger RNA for serum albumin (HSA)	431	392A>G	D131G
V00494	V00494	103600	GEN-TL	Human messenger RNA for serum albumin (HSA)	1090	1051T>C	S
V00494	V00494	103600	GEN-TL	Human messenger RNA for serum albumin (HSA)	1091	1052T>G	L351W
V00494	V00494	103600	GEN-TL	Human messenger RNA for serum albumin (HSA)	1531	1492A>C	T498P
V00494	V00494	103600	GEN-TL	Human messenger RNA for serum albumin (HSA)	1533	1494C>A	S
V00494	V00494	103600	GEN-TL	Human messenger RNA for serum albumin (HSA)	1637	1598T>C	F533S
V00494	V00494	103600	GEN-TL	Human messenger RNA for serum albumin (HSA)	1707	1668C>T	S
V00494	V00494	103600	GEN-TL	Human messenger RNA for serum albumin (HSA)	1719	1680G>A	S
V00494	V00494	103600	GEN-TL	Human messenger RNA for serum albumin (HSA)	1926	1887T>A	3
V00594	V00594	156360	GEN-P6	Human mRNA for metallothionein from cadmium-treated cells	320	263G>C	3
X02317	X02317	147450	GEN-KM	Superoxide dismutase 1 (Cu/Zn)	614	550A>C	3
X02920	X02920	107400	GEN-PH	Human mRNA for alpha 1-	107	107T>C	L36P

X02920	X02920	107400	GEN-PH	antitrypsin carboxyterminal region (aa 268-394)	137	137G>A	S46N
X02920	X02920	107400	GEN-PH	Human mRNA for alpha 1-antitrypsin carboxyterminal region (aa 268-394)	195	195C>T	S
X02920	X02920	107400	GEN-PH	Human mRNA for alpha 1-antitrypsin carboxyterminal region (aa 268-394)	327	327A>C	E109D
X03438	X03438	138970	GEN-PM	Human mRNA for granulocyte colony-stimulating factor (G-CSF)	586	555G>A	S
X03438	X03438	138970	GEN-PM	Human mRNA for granulocyte colony-stimulating factor (G-CSF)	1235	1204C>T	3
X03663	X03663	164770	GEN-51	Colony stimulating factor 1 receptor	3732	3432T>C	3
X03663	X03663	164770	GEN-51	Colony stimulating factor 1 receptor	3951	3651C>A	3
X08006	X08006	None	GEN-1FE	Human mRNA for cytochrome P450 db1	100	100C>T	P34S
X08006	X08006	None	GEN-1FE	Human mRNA for cytochrome P450 db1	124	124G>A	G42R
X08006	X08006	None	GEN-1FE	Human mRNA for cytochrome P450 db1	137	137^138insT	F
X08006	X08006	None	GEN-1FE	Human mRNA for cytochrome P450 db1	271	271C>G	L91V
X08006	X08006	None	GEN-1FE	Human mRNA for cytochrome P450 db1	281	281A>G	H94R
X08006	X08006	None	GEN-1FE	Human mRNA for cytochrome P450 db1	294	294C>G	S
X08006	X08006	None	GEN-1FE	Human mRNA for cytochrome P450 db1	336	336C>T	S
X08006	X08006	None	GEN-1FE	Human mRNA for cytochrome P450 db1	408	408G>C	S
X08006	X08006	None	GEN-1FE	Human mRNA for cytochrome P450 db1	408	408G>C	S
X08006	X08006	None	GEN-1FE	Human mRNA for cytochrome P450 db1	454	454delT	F

X08006	X08006	None	GEN-1FE	Human mRNA for cytochrome P450 db1	505	505G>T	F
X08006	X08006	None	GEN-1FE	Human mRNA for cytochrome P450 db1	635	635G>A	G212E
X08006	X08006	None	GEN-1FE	Human mRNA for cytochrome P450 db1	692	692T>C	L231P
X08006	X08006	None	GEN-1FE	Human mRNA for cytochrome P450 db1	696	696T>C	S
X08006	X08006	None	GEN-1FE	Human mRNA for cytochrome P450 db1	775	775delA	F
X08006	X08006	None	GEN-1FE	Human mRNA for cytochrome P450 db1	801	801C>A	S
X08006	X08006	None	GEN-1FE	Human mRNA for cytochrome P450 db1	836	836T>A	M279K
X08006	X08006	None	GEN-1FE	Human mRNA for cytochrome P450 db1	839	839-841AGA>AG	S
X08006	X08006	None	GEN-1FE	Human mRNA for cytochrome P450 db1	839	839-841delAGA	K281del
X08006	X08006	None	GEN-1FE	Human mRNA for cytochrome P450 db1	840	840-842GAA>GA	S
X08006	X08006	None	GEN-1FE	Human mRNA for cytochrome P450 db1	840	840-842delGAA	K281del
X08006	X08006	None	GEN-1FE	Human mRNA for cytochrome P450 db1	854	854A>G	N285S
X08006	X08006	None	GEN-1FE	Human mRNA for cytochrome P450 db1	886	886C>T	R296C
X08006	X08006	None	GEN-1FE	Human mRNA for cytochrome P450 db1	971	971A>C	H324P
X08006	X08006	None	GEN-1FE	Human mRNA for cytochrome P450 db1	1108	1108G>A	V370I
X08006	X08006	None	GEN-1FE	Human mRNA for cytochrome P450 db1	1203	1203G>A	S
X08006	X08006	None	GEN-1FE	Human mRNA for cytochrome P450 db1	1262	1262T>C	L421P
X08006	X08006	None	GEN-1FE	Human mRNA for cytochrome P450 db1	1401	1401G>C	S
X08006	X08006	None	GEN-1FE	Human mRNA for cytochrome P450 db1	1457	1457G>C	S486T
X08006	X08006	None	GEN-1FE	Human mRNA for cytochrome P450 db1	1457	1457G>C	S486T

X12387	X12387	124010	1FE GEN- 1LZ	cytochrome P450 db1 Human mRNA for cytochrome P-450 (cyp3 locus)	44	(-26)G>C	5
X12387	X12387	124010	GEN- 1LZ	Human mRNA for cytochrome P-450 (cyp3 locus)	628	559A>T	T187S
X12387	X12387	124010	GEN- 1LZ	Human mRNA for cytochrome P-450 (cyp3 locus)	646	577A>G	I193V
X12387	X12387	124010	GEN- 1LZ	Human mRNA for cytochrome P-450 (cyp3 locus)	676	607T>C	F203L
X12387	X12387	124010	GEN- 1LZ	Human mRNA for cytochrome P-450 (cyp3 locus)	823	754T>G	S252A
X12387	X12387	124010	GEN- 1LZ	Human mRNA for cytochrome P-450 (cyp3 locus)	1361	1292T>C	I431T
X12387	X12387	124010	GEN- 1LZ	Human mRNA for cytochrome P-450 (cyp3 locus)	2189	2120G>A	3
X13561	X13561	147910	GEN- 1OH	Human mRNA for preprokallikrein (EC 3.4.21)	54	18G>T	S
X13561	X13561	147910	GEN- 1OH	Human mRNA for preprokallikrein (EC 3.4.21)	441	405T>C	S
X13561	X13561	147910	GEN- 1OH	Human mRNA for preprokallikrein (EC 3.4.21)	469	433G>C	E145Q
X13561	X13561	147910	GEN- 1OH	Human mRNA for preprokallikrein (EC 3.4.21)	592	556A>G	K186E
X13589	X13589	107910	GEN-56	Cytochrome P450, subfamily XIX (aromatization of androgens)	364	240A>G	S
X13589	X13589	107910	GEN-56	Cytochrome P450, subfamily XIX (aromatization of androgens)	914	790C>T	R264C
X13589	X13589	107910	GEN-56	Cytochrome P450, subfamily XIX (aromatization of androgens)	914	790C>T	R264C

X13589	X13589	107910	GEN-56	androgens) Cytochrome P450, subfamily XIX (aromatization of androgens)	1655	1531C>T	3
X13589	X13589	107910	GEN-56	Cytochrome P450, subfamily XIX (aromatization of androgens)	1796	1672G>T	3
X13930	X13930	122720	GEN-1Q3	Human CYP2A4 mRNA for P-450 IIA4 protein	60	51A>G	S
X13930	X13930	122720	GEN-1Q3	Human CYP2A4 mRNA for P-450 IIA4 protein	255	246T>C	S
X13930	X13930	122720	GEN-1Q3	Human CYP2A4 mRNA for P-450 IIA4 protein	272	263G>A	R88K
X13930	X13930	122720	GEN-1Q3	Human CYP2A4 mRNA for P-450 IIA4 protein	1072	1063G>A	V355M
X13930	X13930	122720	GEN-1Q3	Human CYP2A4 mRNA for P-450 IIA4 protein	1146	1137G>A	S
X13930	X13930	122720	GEN-1Q3	Human CYP2A4 mRNA for P-450 IIA4 protein	1485	1476G>T	S
X13930	X13930	122720	GEN-1Q3	Human CYP2A4 mRNA for P-450 IIA4 protein	1675	1666A>T	3
X13930	X13930	122720	GEN-1Q3	Human CYP2A4 mRNA for P-450 IIA4 protein	1677	1668C>G	3
X13930	X13930	122720	GEN-1Q3	Human CYP2A4 mRNA for P-450 IIA4 protein	1697	1688C>A	3
X16699	X16699	124075	GEN-1YJ	Human mRNA for cytochrome P-450HP	1064	1064T>G	F355C
X52773	X52773	180245	GEN-74	Retinoid X receptor, alpha	1744	1669G>A	3
X56199	X56199	None	GEN-36T	Human XIST, coding sequence a mRNA (locus DXS399E)	1338	1339T>G	3
X57522	X57522	170260	GEN-37W	H.sapiens RING4 cDNA	1207	1177A>G	I393V
X57522	X57522	170260	GEN-37W	H.sapiens RING4 cDNA	2120	2090A>G	D697G
X59498	X59498	176300	GEN-RU	H.sapiens ttr mRNA for transthyretin	92	71G>A	G24D
X59498	X59498	176300	GEN-RU	H.sapiens ttr mRNA for transthyretin	177	156G>T	S

X59498	X59498	176300	GEN-RU	H.sapiens ttr mRNA for transthyretin	380	359C>T	S120F
X60069	X60069	231950	GEN-3AJ	Human mRNA for pancreatic gamma-glutamyltransferase	102	(-257)G>A	5
X60069	X60069	231950	GEN-3AJ	Human mRNA for pancreatic gamma-glutamyltransferase	336	(-23)C>T	5
X60069	X60069	231950	GEN-3AJ	Human mRNA for pancreatic gamma-glutamyltransferase	1173	815C>T	A272V
X60069	X60069	231950	GEN-3AJ	Human mRNA for pancreatic gamma-glutamyltransferase	1173	815C>T	A272V
X60069	X60069	231950	GEN-3AJ	Human mRNA for pancreatic gamma-glutamyltransferase	1399	1041C>T	S
X60069	X60069	231950	GEN-3AJ	Human mRNA for pancreatic gamma-glutamyltransferase	1409	1051G>T	A351S
X60069	X60069	231950	GEN-3AJ	Human mRNA for pancreatic gamma-glutamyltransferase	1482	1124C>T	T375M
X60069	X60069	231950	GEN-3AJ	Human mRNA for pancreatic gamma-glutamyltransferase	1591	1233G>A	S
X60069	X60069	231950	GEN-3AJ	Human mRNA for pancreatic gamma-glutamyltransferase	1624	1266C>T	S
X60069	X60069	231950	GEN-3AJ	Human mRNA for pancreatic gamma-glutamyltransferase	1637	1279C>A	P427T
X60069	X60069	231950	GEN-3AJ	Human mRNA for pancreatic gamma-glutamyltransferase	1651	1293C>T	S
X60069	X60069	231950	GEN-3AJ	Human mRNA for pancreatic gamma-glutamyltransferase	1662	1304T>C	V435A
X60069	X60069	231950	GEN-3AJ	Human mRNA for pancreatic gamma-glutamyltransferase	1783	1425A>G	S

X60069	X60069	231950	GEN-3AJ	Human mRNA for pancreatic gamma-glutamyltransferase	1794	1436C>T	T479M
X60069	X60069	231950	GEN-3AJ	Human mRNA for pancreatic gamma-glutamyltransferase	1795	1437G>A	S
X60069	X60069	231950	GEN-3AJ	Human mRNA for pancreatic gamma-glutamyltransferase	1981	1623C>T	S
X60069	X60069	231950	GEN-3AJ	Human mRNA for pancreatic gamma-glutamyltransferase	2007	1649C>T	T550M
X60069	X60069	231950	GEN-3AJ	Human mRNA for pancreatic gamma-glutamyltransferase	2031	1673C>T	S558L
X60069	X60069	231950	GEN-3AJ	Human mRNA for pancreatic gamma-glutamyltransferase	2047	1689C>T	S
X60069	X60069	231950	GEN-3AJ	Human mRNA for pancreatic gamma-glutamyltransferase	2147	1789C>T	3
X60069	X60069	231950	GEN-3AJ	Human mRNA for pancreatic gamma-glutamyltransferase	2176	1818C>T	3
X60069	X60069	231950	GEN-3AJ	Human mRNA for pancreatic gamma-glutamyltransferase	2224	1866C>A	3
X63359	X63359	600070	GEN-3DC	H.sapiens UGT2B10 mRNA for udp glucuronosyltransferase	1516	1506C>T	S
X63359	X63359	600070	GEN-3DC	H.sapiens UGT2B10 mRNA for udp glucuronosyltransferase	2714	2704G>A	3
X63522	X63522	180246	GEN-75	MHC class I promoter binding protein	1331	1152T>C	S
X64177	X64177	156351	GEN-3EQ	H.sapiens mRNA for metallothionein	63	40G>A	A14T
X64177	X64177	156351	GEN-3EQ	H.sapiens mRNA for metallothionein	90	67A>G	K23E
X64177	X64177	156351	GEN-3EQ	H.sapiens mRNA for metallothionein	125	102C>T	S

X64177	X64177	156351	GEN-3EQ	H.sapiens mRNA for metallothionein	131	108T>C	S
X64177	X64177	156351	GEN-3EQ	H.sapiens mRNA for metallothionein	168	145A>G	I49V
X64177	X64177	156351	GEN-3EQ	H.sapiens mRNA for metallothionein	182	159G>A	S
X68836	X68836	601468	GEN-3IR	H.sapiens mRNA for S-adenosylmethionine synthetase	240	175G>A	V59I
X71440	X71440	None	GEN-3KS	H.sapiens mRNA for peroxisomal acyl-CoA oxidase	949	936G>C	M312I
X78282	X78282	601292	GEN-LVF	H.sapiens mRNA for aryl sulfotransferase (ST1A2)	895	895T>C	3
X79389	X79389	600436	GEN-3T7	H.sapiens GSTT1 mRNA	824	824T>C	3
X86681	X86681	602110	GEN-41E	H.sapiens mRNA for nucleolar protein, HNP36	1725	1340G>A	3
X90908	X90908	600422	GEN-LSA	H.sapiens mRNA for I-15P (I-BABP) protein	364	236C>T	T79M
X90999	X90999	138760	GEN-477	H.sapiens mRNA for Glyoxalase II	950	914A>G	3
X95190	X95190	601641	GEN-49Y	H.sapiens mRNA for Branched chain Acyl-CoA Oxidase	1394	1302C>T	S
X95190	X95190	601641	GEN-49Y	H.sapiens mRNA for Branched chain Acyl-CoA Oxidase	1934	1842C>A	S
X96395	X96395	601107	GEN-4AM	H.sapiens mRNA for canalicular multidrug resistance protein	848	811G>T	A271S
X97868	X97868	300003	GEN-LTH	H.sapiens mRNA for arylsulphatase	1652	1582T>C	Y528H
X98332	X98332	602607	GEN-MMA	H.sapiens mRNA for organic cation transporter, liver	630	558C>T	S
XDH	U06117	278300	GEN-194	Human xanthine dehydrogenase (XDH) mRNA, complete cds	3951	3888C>G	S
Y00498	Y00498	601129	GEN-9N	Cytochrome P450, subfamily I1C (mephenytoin	431	389C>A	T130N

Y00498	Y00498	601129	GEN-9N	4-hydroxylase) Cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase)	489	447T>C	S
Y00498	Y00498	601129	GEN-9N	Cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase)	491	449A>G	H150R
Y00498	Y00498	601129	GEN-9N	Cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase)	522	480G>T	K160N
Y00498	Y00498	601129	GEN-9N	Cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase)	525	483T>C	S
Y00498	Y00498	601129	GEN-9N	Cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase)	582	540C>T	S
Y00498	Y00498	601129	GEN-9N	Cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase)	583	541G>A	V181I
Y00498	Y00498	601129	GEN-9N	Cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase)	834	792C>G	I264M
Y00498	Y00498	601129	GEN-9N	Cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase)	999	957C>G	S
Y00498	Y00498	601129	GEN-9N	Cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase)	1539	1497T>C	3

Table 15.
Identified
Variances
In Genes
for
Pathways
Identified
in
Inflammati
on and
Immune
Disease

SD-144146.1

AB00022	AB00022	None	GEN-16K	Homo sapiens mRNA for CC chemokine, complete cds	427	364C>T	3
AB00050	AB00050	602356	GEN-161	Homo sapiens mRNA for TRAF5, complete cds	2185	2131A>T	3
AB00088	AB00088	602227	GEN-14F	Human mRNA for EBI1-ligand chemokine, complete cds	627	489G>A	3
AB00240	AB00240	602737	GEN-1A1	Homo sapiens mRNA for SLC, complete cds	794	736T>G	3
AB02068	AB02068	None	GEN-LAX	Homo sapiens mRNA for KIAA0873 protein, partial cds	3854	3854A>G	3
AC00577	AC00577	None	GEN-ML4	Homo sapiens chromosome 19, cosmid F20237	1492	1482G>A	3
AF000234	AF000234	600846	GEN-16J	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 4; P2RX4	365	365C>T	P122L
AF000234	AF000234	600846	GEN-16J	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 4; P2RX4	381	381G>A	S
AF000234	AF000234	600846	GEN-16J	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 4; P2RX4	624	624A>G	S
AF000234	AF000234	600846	GEN-16J	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 4; P2RX4	641	641C>T	P214L
AF000234	AF000234	600846	GEN-16J	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 4; P2RX4	1161	1161T>C	3
AF000571	AF000571	192500	GEN-15U	K+ channel (KvLQT1)	545	435C>T	S
AF000571	AF000571	192500	GEN-15U	K+ channel (KvLQT1)	1748	1638G>A	S
AF000571	AF000571	192500	GEN-15U	K+ channel (KvLQT1)	2360	2250G>A	3
AF000571	AF000571	192500	GEN-15U	K+ channel (KvLQT1)	2552	2442C>T	3
AF000571	AF000571	192500	GEN-15U	K+ channel (KvLQT1)	3016	2906A>G	3

AF000571	AF000571	192500	GEN-15U	K+ channel (KvLQT1)	3073	2963A>G	3
AF001174	AF001174	602898	GEN-18T	Homo sapiens p38beta2 MAP kinase mRNA, complete cds	1044	1038T>C	S
AF004709	AF004709	602899	GEN-UX	Homo sapiens stress-activated protein kinase 4 mRNA, complete cds	432	384G>A	S
AF006689	AF006689	603014	GEN-YA	Homo sapiens MAP kinase kinase Jnk2 mRNA, complete cds	75	(-1)G>A	5
AF009620	AF009620	601763	GEN-1HV	Homo sapiens apoptotic caspase Mch5-beta mRNA, alternatively spliced, complete cds	808	808C>G	H270D
AF009620	AF009620	601763	GEN-1HV	Homo sapiens apoptotic caspase Mch5-beta mRNA, alternatively spliced, complete cds	915	915G>A	S
AF012535	AF012535	None	GEN-1Z2	Homo sapiens death receptor 5 (DR5) mRNA, complete cds	234	95T>C	L32P
AF012535	AF012535	None	GEN-1Z2	Homo sapiens death receptor 5 (DR5) mRNA, complete cds	339	200C>T	A67V
AF012535	AF012535	None	GEN-1Z2	Homo sapiens death receptor 5 (DR5) mRNA, complete cds	1397	1258G>C	3
AF016709	AF016709	602836	GEN-1NE	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 5; P2RX5	1023	987T>C	S
AF016709	AF016709	602836	GEN-1NE	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 5; P2RX5	1025	989T>C	F330S
AF016709	AF016709	602836	GEN-1NE	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 5; P2RX5	1090	1054G>C	E352Q
AF016709	AF016709	602836	GEN-1NE	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 5; P2RX5	1321	1285G>A	3

AF016709	AF016709	602836	GEN- 1NE	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 5; P2RX5	1424	1388C>G	3
AF016709	AF016709	602836	GEN- 1NE	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 5; P2RX5	1512	1476G>A	3
AF016709	AF016709	602836	GEN- 1NE	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 5; P2RX5	1743	1707A>G	3
AF016709	AF016709	602836	GEN- 1NE	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 5; P2RX5	1858	1822A>G	3
AF021792	AF021792	603167	GEN- 2A5	Homo sapiens Bcl-X/Bcl-2 binding protein (BAD) mRNA, partial cds	781	781G>A	3
AF021792	AF021792	603167	GEN- 2A5	Homo sapiens Bcl-X/Bcl-2 binding protein (BAD) mRNA, partial cds	883	883C>A	3
AF026070	AF026070	None	GEN- 26S	Homo sapiens death receptor 3 beta (DR3) mRNA, complete cds	455	387A>G	S
AF026070	AF026070	None	GEN- 26S	Homo sapiens death receptor 3 beta (DR3) mRNA, complete cds	1202	1134T>C	S
AF026070	AF026070	None	GEN- 26S	Homo sapiens death receptor 3 beta (DR3) mRNA, complete cds	1204	1136T>G	L379R
AF026070	AF026070	None	GEN- 26S	Homo sapiens death receptor 3 beta (DR3) mRNA, complete cds	1237	1169A>G	H390R
HRH1	AF026261	600167	GEN- 26W	Histamine receptor H1	1068	1068A>G	S
AF029761	AF029761	None	GEN- MND	Homo sapiens decoy receptor 2 mRNA, complete cds	1011	929C>T	S310L
ITGA7	AF032108	600536	GEN- 2NO	Homo sapiens integrin alpha-7 mRNA, complete cds	527	366G>A	S
TUBB	AF035316	191130	GEN-2IH	Homo sapiens clone 23678 mRNA, partial cds	273	273G>A	F
TUBB	AF035316	191130	GEN-2IH	Homo sapiens clone 23678	295	295G>C	A99P

TUBB	AF035316	191130	GEN-2IH	Homo sapiens clone 23678 mRNA, partial cds	302	302C>T	T101I
TUBB	AF035316	191130	GEN-2IH	Homo sapiens clone 23678 mRNA, partial cds	1059	1059G>A	3
AF039400	AF039400	603906	GEN-MQY	Homo sapiens calcium-dependent chloride channel-1 (hCLCA1) mRNA, complete cds	2787	2436T>C	S
AF043472	AF043472	603888	GEN-2XX	Homo sapiens Shab-related delayed-rectifier K ⁺ channel alpha subunit (KCNS3) mRNA, complete cds	1840	1709T>G	3
AF048837	AF048837	602973	GEN-LGG	Homo sapiens cGMP-specific phosphodiesterase (PDE9A2) mRNA, complete cds	1551	1491T>C	S
AF053712	AF053712	None	GEN-MM2	Homo sapiens osteoprotegerin ligand mRNA, complete cds	2086	1902T>G	3
AF058921	AF058921	None	GEN-LJY	Homo sapiens cytosolic phospholipase A2-gamma mRNA, complete cds	1972	1663G>A	3
AF058921	AF058921	None	GEN-LJY	Homo sapiens cytosolic phospholipase A2-gamma mRNA, complete cds	1989	1680A>T	3
AF065164	AF065164	None	GEN-LKQ	Homo sapiens hyperpolarization-activated channel 1 (IH1) mRNA, partial cds	1980	1860T>C	S
AF094760	AF094760	None	GEN-LSB	Homo sapiens RFXANK (RFXANK) mRNA, complete cds	1038	621G>A	S
AF094760	AF094760	None	GEN-LSB	Homo sapiens RFXANK (RFXANK) mRNA, complete cds	1071	654C>T	S
D00017	D00017	151740	GEN-2D	Lipocortin II (Annexin II)	149	100G>A	D34N
D00017	D00017	151740	GEN-2D	Lipocortin II (Annexin II)	341	292G>T	V98L
D00017	D00017	151740	GEN-2D	Lipocortin II (Annexin II)	479	430A>T	N144Y

D00017	D00017	151740	GEN-2D	Lipocortin II (Annexin II)	1288	1239G>A	3
D12614	D12614	153440	GEN-QD	Human mRNA for lymphotoxin (TNF-beta), complete cds	319	179C>A	T60N
D13138	D13138	179780	GEN-1NW	Human mRNA for dipeptidase	566	523T>G	S175A
CYP11B2	D13752	124080	GEN-CCD	Human CYP11B2 gene for steroid 18-hydroxylase, complete cds	1600	1593G>A	3
D13811	D13811	238310	GEN-AA	Glycine cleavage system: Protein T	277	148G>T	V50L
D13811	D13811	238310	GEN-AA	Glycine cleavage system: Protein T	1073	944G>A	R315K
D13811	D13811	238310	GEN-AA	Glycine cleavage system: Protein T	1083	954G>A	S
D13811	D13811	238310	GEN-AA	Glycine cleavage system: Protein T	1773	1644C>T	3
D13811	D13811	238310	GEN-AA	Glycine cleavage system: Protein T	2037	1908C>T	3
D25235	D25235	104221	GEN-3	Adrenergic receptor alpha 1c	1035	599T>G	I200S
D25235	D25235	104221	GEN-3	Adrenergic receptor alpha 1c	1475	1039C>T	R347C
D25235	D25235	104221	GEN-3	Adrenergic receptor alpha 1c	1475	1039C>T	R347C
D25235	D25235	104221	GEN-3	Adrenergic receptor alpha 1c	2048	1612C>T	3
D25418	D25418	600022	GEN-78	Prostaglandin I2 (prostaglandin) receptor (IP)	726	635G>A	R212H
D25418	D25418	600022	GEN-78	Prostaglandin I2 (prostaglandin) receptor (IP)	1047	956C>G	S319W
D25418	D25418	600022	GEN-78	Prostaglandin I2 (prostaglandin) receptor (IP)	1075	984A>C	S
D26579	D26579	602267	GEN-2B1	Human mRNA for transmembrane protein, complete cds	709	700G>A	D234N
D26579	D26579	602267	GEN-2B1	Human mRNA for transmembrane protein, complete cds	909	900T>C	S
D26579	D26579	602267	GEN-2B1	Human mRNA for transmembrane protein, complete cds	999	990C>T	S

D26579	D26579	602267	GEN-2B1	complete cds Human mRNA for transmembrane protein,	1104	1095A>G	S
D32051	D32051	138440	GEN-4	complete cds Glycinamide ribonucleotide transformylase	25	(-47)G>A	5
D32051	D32051	138440	GEN-4	Glycinamide ribonucleotide transformylase	1332	1261A>G	I421V
D32051	D32051	138440	GEN-4	Glycinamide ribonucleotide transformylase	1855	1784G>C	3
PTGIR	D38128	600022	GEN-4DH	Human IP gene for prostacyclin receptor, exon 3	203	204C>G	3
PTGIR	D38128	600022	GEN-4DH	Human IP gene for prostacyclin receptor, exon 3	231	232C>A	3
D38145	D38145	601699	GEN-4E3	Human mRNA for prostacyclin synthase, complete cds	1646	1619T>C	3
NT5	D38524	129190	GEN-2PF	Human mRNA for 5-nucleotidase	3075	2992C>T	3
D42108	D42108	600597	GEN-2U4	Phospholipase C epsilon	1908	1705G>A	V569I
D42108	D42108	600597	GEN-2U4	Phospholipase C epsilon	2864	2661G>A	S
D42108	D42108	600597	GEN-2U4	Phospholipase C epsilon	4453	4250G>A	3
D45887	D45887	114182	GEN-BA	Calmodulin 1 (phosphorylase kinase, delta)	34	(-35)G>T	5
D49737	D49737	602413	GEN-2Z7	Homo sapiens mRNA for cytochrome b large subunit of complex II, complete cds	908	784G>A	3
D86955	D86955	601960	GEN-41O	Human mRNA for CC chemokine LARC precursor, complete cds	328	270T>C	S
D87461	D87461	601931	GEN-43N	Human mRNA for KIAA0271 gene, complete cds	2432	2256C>A	3
D87845	D87845	602344	GEN-44C	Human mRNA for platelet-activating factor	2299	2096G>A	3

D87845	D87845	602344	GEN-44C	Human mRNA for platelet-activating factor acetylhydrolase 2, complete cds	2332	2129A>G	3
D89078	D89078	601531	GEN-7	P2Y7 purinoceptor	434	(-1284)A>T	5
D89078	D89078	601531	GEN-7	P2Y7 purinoceptor	889	(-829)G>C	5
D89078	D89078	601531	GEN-7	P2Y7 purinoceptor	1156	(-562)G>C	5
D89078	D89078	601531	GEN-7	P2Y7 purinoceptor	2644	927T>C	S
D89078	D89078	601531	GEN-7	P2Y7 purinoceptor	2920	1203A>G	3
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	1449	969C>T	S
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	1449	969C>T	S
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	1485	1005A>G	S
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	1485	1005A>G	S
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	1834	1354C>G	3
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	1834	1354C>G	3
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	2228	1748G>A	3
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	2376	1896G>A	3
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	2764	2284G>A	3
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	2764	2284G>A	3
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	2840	2360G>C	3
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	2935	2455G>A	3
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	3294	2814A>G	3
J00123	J00123	131330	GEN-MK4	Human enkephalin gene	81	81C>T	S
DHFR	J00140	126060	GEN-	Human dihydrofolate	721	679T>A	3

DHFR	J00140	126060	4E9 GEN-4E9	reductase gene Human dihydrofolate reductase gene	721	679T>A	3
DHFR	J00140	126060	GEN-4E9	Human dihydrofolate reductase gene	829	787C>T	3
CBG	J02943	122500	GEN-Y2	Human corticosteroid binding globulin mRNA, complete cds	106	71A>T	D24V
CBG	J02943	122500	GEN-Y2	Human corticosteroid binding globulin mRNA, complete cds	971	936T>C	S
CBG	J02943	122500	GEN-Y2	Human corticosteroid binding globulin mRNA, complete cds	1229	1194G>A	S
J03004	J03004	139360	GEN-79	Guanine nucleotide binding protein (G protein), alpha inhibiting activity	758	681C>T	S
J03019	J03019	109630	GEN-4D6	polypeptide 2 Human beta-1-adrenergic receptor mRNA, complete cds	503	417G>A	S
J03143	J03143	107470	GEN-ZK	Human interferon-gamma receptor mRNA, complete cds	1098	1050T>G	S
J03209	J03209	185250	GEN-PK	Human matrix metalloproteinase-3 (MMP-3) mRNA, complete cds	133	133G>A	E45K
J03209	J03209	185250	GEN-PK	Human matrix metalloproteinase-3 (MMP-3) mRNA, complete cds	288	288C>T	S
J03210	J03210	120360	GEN-ZY	Human collagenase type IV mRNA, 3 end	721	721C>T	P241S
J03210	J03210	120360	GEN-ZY	Human collagenase type IV mRNA, 3 end	1759	1759C>T	P587S
J03250	J03250	172420	GEN-C4	DNA topoisomerase I	160	(-52)C>T	5
J03250	J03250	172420	GEN-C4	DNA topoisomerase I	590	379G>A	V127I
J03250	J03250	172420	GEN-C4	DNA topoisomerase I	1984	1773G>A	S
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	172	57C>T	S

J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	559	444C>T	S
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	1704	1589C>A	3
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	1833	1718C>G	3
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	1858	1743G>T	3
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	1959	1844A>C	3
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	2190	2075delT	F
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	3301	3186C>A	3
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	3991	3876A>G	3
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	4187	4072G>A	3
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	4187	4072G>A	3
J03459	J03459	151570	GEN-8	Leukotriene A4 hydrolase	140	72G>T	S
J03459	J03459	151570	GEN-8	Leukotriene A4 hydrolase	1511	1443A>T	E481D
C7	J03507	217070	GEN-11R	Human complement protein component C7 mRNA, complete cds	1951	1951G>A	V651I
C7	J03507	217070	GEN-11R	Human complement protein component C7 mRNA, complete cds	3032	3032T>C	3
C7	J03507	217070	GEN-11R	Human complement protein component C7 mRNA, complete cds	3634	3634A>G	3

C7	J03507	217070	GEN-11R	Human complement protein component C7 mRNA, complete cds	3831	3831A>G	3
J03571	J03571	152390	GEN-9	Lipoxygenases: 5-lipoxygenase (leukocytes)	55	21C>T	S
J03571	J03571	152390	GEN-9	Lipoxygenases: 5-lipoxygenase (leukocytes)	304	270G>A	S
J03571	J03571	152390	GEN-9	Lipoxygenases: 5-lipoxygenase (leukocytes)	304	270G>A	S
J03571	J03571	152390	GEN-9	Lipoxygenases: 5-lipoxygenase (leukocytes)	959	925C>A	P309T
J03571	J03571	152390	GEN-9	Lipoxygenases: 5-lipoxygenase (leukocytes)	1762	1728A>T	S
J03571	J03571	152390	GEN-9	Lipoxygenases: 5-lipoxygenase (leukocytes)	2076	2042-2043AC>AC	3
J03571	J03571	152390	GEN-9	Lipoxygenases: 5-lipoxygenase (leukocytes)	2076	2042-2043delAC	F
J03571	J03571	152390	GEN-9	Lipoxygenases: 5-lipoxygenase (leukocytes)	2328	2294C>T	3
J03571	J03571	152390	GEN-9	Lipoxygenases: 5-lipoxygenase (leukocytes)	2376	2342T>G	3
PTHLH	J03580	168470	GEN-11U	Lipoxygenase (leukocytes) Human, parathyroid-like protein (associated with humoral hypercalcemia of malignancy) mRNA, complete cds	975	37G>A	V13M
PTHLH	J03580	168470	GEN-11U	Human, parathyroid-like protein (associated with humoral hypercalcemia of malignancy) mRNA, complete cds	996	58G>A	V20M
J03853	J03853	104250	GEN-A	Adrenergic receptor alpha _{2c}	1202	1164C>T	S
J03853	J03853	104250	GEN-A	Adrenergic receptor alpha _{2c}	1237	1199T>G	I400S
J03853	J03853	104250	GEN-A	Adrenergic receptor alpha _{2c}	1372	1334C>G	P445R
J03853	J03853	104250	GEN-A	Adrenergic receptor alpha _{2c}	1379	1341C>T	S
J04031	J04031	172460	GEN-CB	Methylenetetrahydrofolate cyclohydrolase	454	401G>A	R134K

J04031	J04031	172460	GEN-CB	Methenyltetrahydrofolate cyclohydrolase	969	916C>G	Q306E
J04031	J04031	172460	GEN-CB	Methenyltetrahydrofolate cyclohydrolase	1614	1561T>C	S
J04031	J04031	172460	GEN-CB	Methenyltetrahydrofolate cyclohydrolase	2011	1958G>A	R653Q
J04031	J04031	172460	GEN-CB	Methenyltetrahydrofolate cyclohydrolase	2335	2282C>T	T761M
J04046	J04046	114183	GEN- 13N	Human calmodulin mRNA, complete cds	791	688C>T	3
J04046	J04046	114183	GEN- 13N	Human calmodulin mRNA, complete cds	881	778T>C	3
J04046	J04046	114183	GEN- 13N	Human calmodulin mRNA, complete cds	1927	1824T>C	3
C1S	J04080	120580	GEN- 13T	Complement C1S component precursor (C1 esterase)	558	356G>A	R119H
C1S	J04080	120580	GEN- 13T	Complement C1S component precursor (C1 esterase)	2140	1938A>T	K646N
C1S	J04080	120580	GEN- 13T	Complement C1S component precursor (C1 esterase)	2234	2032A>T	T678S
C1S	J04080	120580	GEN- 13T	Complement C1S component precursor (C1 esterase)	2333	2131G>T	3
J04132	J04132	186780	GEN- KXY	Human T cell receptor zeta-chain mRNA, complete cds	1403	1329G>C	3
J04132	J04132	186780	GEN- KXY	Human T cell receptor zeta-chain mRNA, complete cds	1410	1336A>T	3
J04145	J04145	120980	GEN-B	Leukocyte integrin alpha-m	206	206G>A	R69H
J04145	J04145	120980	GEN-B	Leukocyte integrin alpha-m	1780	1780C>T	S
J04145	J04145	120980	GEN-B	Leukocyte integrin alpha-m	2478	2478G>A	S
J04145	J04145	120980	GEN-B	Leukocyte integrin alpha-m	2978	2978C>A	T993N
J04145	J04145	120980	GEN-B	Leukocyte integrin alpha-m	3415	3415C>T	P1139S
J04145	J04145	120980	GEN-B	Leukocyte integrin alpha-m	3661	3661C>T	3
J04145	J04145	120980	GEN-B	Leukocyte integrin alpha-m	3804	3804A>G	3
J04145	J04145	120980	GEN-B	Leukocyte integrin alpha-m	4071	4071G>A	3

SPN	J04168	182160	GEN-13W	Human leukosialin mRNA, complete cds	974	879C>T	S
SPN	J04168	182160	GEN-13W	Human leukosialin mRNA, complete cds	1328	1233G>C	3
J04208	J04208	146691	GEN-2M	IMP (inosine monophosphate) dehydrogenase 2	349	302C>G	A101G
J04208	J04208	146691	GEN-2M	IMP (inosine monophosphate) dehydrogenase 2	1570	1523C>T	S508L
G22P1	J04611	152690	GEN-153	Human lupus p70 (Ku) autoantigen protein mRNA, complete cds	1762	1729A>T	T577S
G22P1	J04611	152690	GEN-153	Human lupus p70 (Ku) autoantigen protein mRNA, complete cds	1812	1779T>G	S
G22P1	J04611	152690	GEN-153	Human lupus p70 (Ku) autoantigen protein mRNA, complete cds	1900	1867G>T	3
BPI	J04739	109195	GEN-15B	Human bactericidal permeability increasing protein (BPI) mRNA, complete cds	1525	1495G>A	3
C6	J05064	217050	GEN-16S	Human complement component C6 mRNA, complete cds	3281	3126G>A	3
J05480	J05480	114105	GEN-D	Calcineurin A	834	834A>G	3
J05594	J05594	601688	GEN-E	Prostaglandin 15-OH dehydrogenase (PGDH)	173	156A>G	S
J05594	J05594	601688	GEN-E	Prostaglandin 15-OH dehydrogenase (PGDH)	913	896C>G	3
J05594	J05594	601688	GEN-E	Prostaglandin 15-OH dehydrogenase (PGDH)	950	933G>A	3
J05594	J05594	601688	GEN-E	Prostaglandin 15-OH dehydrogenase (PGDH)	1448	1431G>A	3
J05594	J05594	601688	GEN-E	Prostaglandin 15-OH dehydrogenase (PGDH)	1972	1955T>C	3
J05594	J05594	601688	GEN-E	Prostaglandin 15-OH dehydrogenase (PGDH)	1972	1955T>C	3
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles)	112	52G>A	A18T

K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	121	61G>A	E21K
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	151	91G>A	E31K
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	197	137T>C	L46P
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	204	144delG	F
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	238	178A>G	T60A
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	365	305C>G	P102R
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	409	349G>A	A117T
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	448	388T>C	C130R
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	494	434G>A	G145D
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	515	455G>A	R152Q
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	520	460C>A	R154S
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	538	478C>T	R160C
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	547	487C>T	R163C
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	548	488G>A	R163H

K00396	K00396	107741	GEN-P0	(epsilon 2 and 3 alleles) mRNA	550	490A>G	K164E
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	586	526C>T	R176C
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	586	526C>T	R176C
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	743	683G>A	F
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	785	725G>A	R242Q
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	796	736C>T	R246C
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	821	761T>A	V254E
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	865	805C>G	R269G
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	935	875G>A	R292H
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	1000	940A>C	S314R
K01171	K01171	None	GEN-PB	Human HLA-DR alpha- chain mRNA	297	283T>C	S
K01171	K01171	None	GEN-PB	Human HLA-DR alpha- chain mRNA	416	402C>A	S
K01171	K01171	None	GEN-PB	Human HLA-DR alpha- chain mRNA	665	651C>T	S
K01171	K01171	None	GEN-PB	Human HLA-DR alpha- chain mRNA	738	724G>T	V242L
K01171	K01171	None	GEN-PB	Human HLA-DR alpha- chain mRNA	748	734G>A	S245N

K01171	K01171	None	GEN-PB	Human HLA-DR alpha-chain mRNA	797	783A>G	3
K01171	K01171	None	GEN-PB	Human HLA-DR alpha-chain mRNA	842	828A>G	3
K01171	K01171	None	GEN-PB	Human HLA-DR alpha-chain mRNA	901	887G>A	3
K01171	K01171	None	GEN-PB	Human HLA-DR alpha-chain mRNA	928	914T>A	3
K01171	K01171	None	GEN-PB	Human HLA-DR alpha-chain mRNA	933	919T>A	3
K01171	K01171	None	GEN-PB	Human HLA-DR alpha-chain mRNA	942	928C>T	3
K01171	K01171	None	GEN-PB	Human HLA-DR alpha-chain mRNA	954	940G>A	3
K01171	K01171	None	GEN-PB	Human HLA-DR alpha-chain mRNA	999	985T>G	3
K01171	K01171	None	GEN-PB	Human HLA-DR alpha-chain mRNA	1035	1021A>C	3
K01171	K01171	None	GEN-PB	Human HLA-DR alpha-chain mRNA	1077	1063C>T	3
K01171	K01171	None	GEN-PB	Human HLA-DR alpha-chain mRNA	1091	1077C>G	3
K01171	K01171	None	GEN-PB	Human HLA-DR alpha-chain mRNA	1154	1140A>C	3
K01171	K01171	None	GEN-PB	Human HLA-DR alpha-chain mRNA	1171	1157T>A	3
KNG	K02566	228960	GEN-X2	Human alpha-2-thiol proteinase inhibitor mRNA, complete coding sequence	1248	1199C>A	T400K
K02765	K02765	120700	GEN-XM	Human complement component C3 mRNA, alpha and beta subunits, complete cds	1001	941T>C	L314P
K02765	K02765	120700	GEN-XM	Human complement component C3 mRNA, alpha and beta subunits, complete cds	2575	2515G>A	V839I
K02765	K02765	120700	GEN-XM	Human complement component C3 mRNA, alpha and beta subunits, complete cds	3108	3048C>T	S

K02765	K02765	120700	GEN-XM	complete cds	3561	3501C>G	S
				Human complement component C3 mRNA, alpha and beta subunits, complete cds			
K02765	K02765	120700	GEN-XM	Human complement component C3 mRNA, alpha and beta subunits, complete cds	4371	4311C>T	S
K02765	K02765	120700	GEN-XM	Human complement component C3 mRNA, alpha and beta subunits, complete cds	4544	4484C>A	P1495Q
K02765	K02765	120700	GEN-XM	Human complement component C3 mRNA, alpha and beta subunits, complete cds	4938	4878T>C	S
K02765	K02765	120700	GEN-XM	Human complement component C3 mRNA, alpha and beta subunits, complete cds	4956	4896T>C	S
K02770	K02770	147720	GEN-5M	Interleukin 1, beta	19	(-68)A>C	5
K02770	K02770	147720	GEN-5M	Interleukin 1, beta	26	(-61)A>C	5
K02770	K02770	147720	GEN-5M	Interleukin 1, beta	48	(-39)C>T	5
K02770	K02770	147720	GEN-5M	Interleukin 1, beta	114	28G>A	E10K
K02770	K02770	147720	GEN-5M	Interleukin 1, beta	119	33G>A	M11I
L01087	L01087	600448	GEN-CM	Protein kinase C-theta	1940	1846C>A	S
L01087	L01087	600448	GEN-CM	Protein kinase C-theta	1943	1849G>A	E617K
L04270	L04270	600979	GEN-144	Homo sapiens (clone CD18) tumor necrosis factor receptor 2 related protein mRNA, complete cds	1478	1310G>T	3
L05148	L05148	176947	GEN-KYC	Human protein tyrosine kinase related mRNA sequence	1886	1887G>A	3
L05597	L05597	None	GEN-4EV	Serotonin 5-HT receptors 5-HT1F	824	600T>C	S
L05597	L05597	None	GEN-4EV	Serotonin 5-HT receptors 5-HT1F	1010	786^787insA ATAAAATTC	[H262Q;26 2^263insl

EDNRB	L06623	131244	GEN-19S	Endothelin Receptor Type B	88	AT (-146)A>G	KFIJ 5
EDNRB	L06623	131244	GEN-19S	Endothelin Receptor Type B	332	99C>T	S
EDNRB	L06623	131244	GEN-19S	Endothelin Receptor Type B	1064	831G>A	S
EDNRB	L06623	131244	GEN-19S	Endothelin Receptor Type B	1064	831G>A	S
TGFBR3	L07594	600742	GEN-1EA	Human transforming growth factor-beta type III receptor (TGF-beta) mRNA, complete cds	3966	3618G>C	3
L07861	L07861	176977	GEN-D0	Protein kinase C, delta	445	387G>A	S
L07861	L07861	176977	GEN-D0	Protein kinase C, delta	1835	1777G>A	V593M
CCKBR	L08112	118445	GEN-1FL	Cholecystokinin (CCKb)	456	456G>A	S
MIF	L10612	153620	GEN-1J8	Human glycosylation-inhibiting factor mRNA, complete cds	170	96C>G	S
MIF	L10612	153620	GEN-1J8	Human glycosylation-inhibiting factor mRNA, complete cds	221	147C>G	S
MIF	L10612	153620	GEN-1J8	Human glycosylation-inhibiting factor mRNA, complete cds	227	153C>G	S
MIF	L10612	153620	GEN-1J8	Human glycosylation-inhibiting factor mRNA, complete cds	239	165G>A	S
MIF	L10612	153620	GEN-1J8	Human glycosylation-inhibiting factor mRNA, complete cds	329	255C>A	S
MIF	L10612	153620	GEN-1J8	Human glycosylation-inhibiting factor mRNA, complete cds	445	371C>T	3
L10717	L10717	186973	GEN-1JB	Homo sapiens T cell-specific tyrosine kinase mRNA, complete cds	856	(-1168)G>A	5
L10717	L10717	186973	GEN-1JB	Homo sapiens T cell-specific tyrosine kinase mRNA, complete cds	1472	(-552)G>A	5

L10717	L10717	186973	GEN-1JB	Homo sapiens T cell-specific tyrosine kinase mRNA, complete cds	4897	2874G>A	3
L10717	L10717	186973	GEN-1JB	Homo sapiens T cell-specific tyrosine kinase mRNA, complete cds	5625	3602G>C	3
L10717	L10717	186973	GEN-1JB	Homo sapiens T cell-specific tyrosine kinase mRNA, complete cds	5628	3605A>C	3
L10819	L10819	171150	GEN-LVD	Homo sapiens aryl sulfotransferase mRNA, complete cds	191	153C>T	S
L10819	L10819	171150	GEN-LVD	Homo sapiens aryl sulfotransferase mRNA, complete cds	200	162G>A	S
L10819	L10819	171150	GEN-LVD	Homo sapiens aryl sulfotransferase mRNA, complete cds	230	192T>C	S
L10819	L10819	171150	GEN-LVD	Homo sapiens aryl sulfotransferase mRNA, complete cds	242	204G>A	S
L10819	L10819	171150	GEN-LVD	Homo sapiens aryl sulfotransferase mRNA, complete cds	295	257C>T	A86V
L10819	L10819	171150	GEN-LVD	Homo sapiens aryl sulfotransferase mRNA, complete cds	330	292G>A	D98N
L10819	L10819	171150	GEN-LVD	Homo sapiens aryl sulfotransferase mRNA, complete cds	338	300G>A	S
L10819	L10819	171150	GEN-LVD	Homo sapiens aryl sulfotransferase mRNA, complete cds	638	600C>G	S
L10819	L10819	171150	GEN-LVD	Homo sapiens aryl sulfotransferase mRNA, complete cds	676	638A>G	H213R
L10819	L10819	171150	GEN-LVD	Homo sapiens aryl sulfotransferase mRNA, complete cds	940	902G>A	3
L10819	L10819	171150	GEN-LVD	Homo sapiens aryl sulfotransferase mRNA, complete cds	1011	973T>C	3

L11005	L11005	602841	GEN-1JU	complete cds Human aldehyde oxidase (hAOX) mRNA, complete cds	4284	4154C>A	3
L11005	L11005	602841	GEN-1JU	Human aldehyde oxidase (hAOX) mRNA, complete cds	4447	4317G>C	3
L11005	L11005	602841	GEN-1JU	Human aldehyde oxidase (hAOX) mRNA, complete cds	4525	4395T>G	3
L11005	L11005	602841	GEN-1JU	Human aldehyde oxidase (hAOX) mRNA, complete cds	4675	4545G>A	3
C4BPB	L11244	120831	GEN-1K2	Human (clone A12) C4b-binding protein beta-chain mRNA, complete cds	538	204G>A	S
C4BPB	L11244	120831	GEN-1K2	Human (clone A12) C4b-binding protein beta-chain mRNA, complete cds	796	462C>T	S
C4BPB	L11244	120831	GEN-1K2	Human (clone A12) C4b-binding protein beta-chain mRNA, complete cds	958	624C>A	S
L11284	L11284	176872	GEN-1K8	Homosapiens ERK activator kinase (MEK1) mRNA	1763	1764T>C	3
L11284	L11284	176872	GEN-1K8	Homosapiens ERK activator kinase (MEK1) mRNA	1914	1915G>A	3
L11285	L11285	601263	GEN-1K7	Homosapiens ERK activator kinase (MEK2) mRNA	252	253C>A	3
L11285	L11285	601263	GEN-1K7	Homosapiens ERK activator kinase (MEK2) mRNA	276	277T>C	3
L11285	L11285	601263	GEN-1K7	Homosapiens ERK activator kinase (MEK2) mRNA	537	538C>T	3
L11285	L11285	601263	GEN-1K7	Homosapiens ERK activator kinase (MEK2) mRNA	613	614G>C	3
L11285	L11285	601263	GEN-	Homosapiens ERK activator kinase (MEK2) mRNA	744	745A>C	3

L11285	L11285	601263	GEN-1K7	1K7	activator kinase (MEK2) mRNA	1156	1157G>T	3
L11285	L11285	601263	GEN-1K7	1K7	Homosapiens ERK activator kinase (MEK2) mRNA	1311	1312C>T	3
L11285	L11285	601263	GEN-1K7	1K7	Homosapiens ERK activator kinase (MEK2) mRNA	1457	1458C>A	3
L11285	L11285	601263	GEN-1K7	1K7	Homosapiens ERK activator kinase (MEK2) mRNA	1459	1460A>C	3
L11667	L11667	601753	GEN-H	GEN-H	Cyclophilin D 40kDa mRNA	1003	904C>A	L302I
L11667	L11667	601753	GEN-H	GEN-H	Cyclophilin D 40kDa	1283	1184A>G	3
L11667	L11667	601753	GEN-H	GEN-H	Cyclophilin D 40kDa	1479	1380T>A	3
L11667	L11667	601753	GEN-H	GEN-H	Cyclophilin D 40kDa	1519	1420T>C	3
L11931	L11931	182144	GEN-4DT	4DT	Human cytosolic serine hydroxymethyltransferase (SHMT) mRNA, complete cds	1444	1420C>T	L474F
L11931	L11931	182144	GEN-4DT	4DT	Human cytosolic serine hydroxymethyltransferase (SHMT) mRNA, complete cds	1541	1517C>T	3
L12052	L12052	171885	GEN-1LK	1LK	Human cAMP phosphodiesterase mRNA, 3 end	1707	1707G>A	3
L12691	L12691	125220	GEN-ST	GEN-ST	Human neutrophil peptide-3 gene, complete cds	244	194A>C	D65A
L12691	L12691	125220	GEN-ST	GEN-ST	Human neutrophil peptide-3 gene, complete cds	433	383T>C	3
MDCR	L13385	601545	GEN-106	106	Homo sapiens(clone 71) Miller-Dieker lissencephaly protein (LIS1) mRNA, complete cds	1467	1250C>T	3
MDCR	L13385	601545	GEN-106	106	Homo sapiens(clone 71) Miller-Dieker lissencephaly protein (LIS1) mRNA, complete cds	1868	1651C>T	3

MDCR	L13385	601545	GEN-106	Homo sapiens(clone 71) Miller-Dieker lissencephaly protein (LIS1) mRNA, complete cds	1917	1700C>T	3
MDCR	L13385	601545	GEN-106	Homo sapiens(clone 71) Miller-Dieker lissencephaly protein (LIS1) mRNA, complete cds	2962	2745G>T	3
MDCR	L13385	601545	GEN-106	Homo sapiens(clone 71) Miller-Dieker lissencephaly protein (LIS1) mRNA, complete cds	4589	4372G>A	3
L14754	L14754	600502	GEN-D9	DNA-binding protein (SMBP2)	2129	2080C>T	R694W
L14754	L14754	600502	GEN-D9	DNA-binding protein (SMBP2)	2365	2316C>T	S
L14754	L14754	600502	GEN-D9	DNA-binding protein (SMBP2)	3696	3647C>T	3
L14754	L14754	600502	GEN-D9	DNA-binding protein (SMBP2)	3712	3663T>C	3
L14754	L14754	600502	GEN-D9	DNA-binding protein (SMBP2)	3771	3722C>G	3
BF	L15702	138470	GEN-1UA	Human complement factor B mRNA, complete cds	135	95A>G	Q32R
L19067	L19067	164014	GEN-DE	TRANSCRIPTION FACTOR P65	1129	1091C>T	S364L
L19956	L19956	600641	GEN-LVE	Human aryl sulfotransferase mRNA, complete cds	243	105A>G	S
L19956	L19956	600641	GEN-LVE	Human aryl sulfotransferase mRNA, complete cds	284	146C>T	S49F
L20298	L20298	121360	GEN-DH	Transcription Factor (CBFB)	2696	2696A>G	3
L20463	L20463	600445	GEN-M	G-protein coupled adenosine A3 receptor	1671	1380A>G	3
L22214	L22214	102775	GEN-2S	Adenosine A1 receptor (ADORA1)	557	147G>C	S
L22214	L22214	102775	GEN-2S	Adenosine A1 receptor (ADORA1)	2622	2212G>A	3
L22473	L22473	600040	GEN-	Human Bax alpha mRNA,	552	552G>A	S

SLC6A3	L24178	126455	L9D GEN-283	complete cds Homo sapiens dopamine transporter mRNA,	1917	1898C>T	3
L24470	L24470	600563	GEN-O	complete cds PROSTAGLANDIN F RECEPTOR	1422	1185T>C	3
L24470	L24470	600563	GEN-O	PROSTAGLANDIN F RECEPTOR	1490	1253C>T	3
L24470	L24470	600563	GEN-O	PROSTAGLANDIN F RECEPTOR	1517	1280A>G	3
L24470	L24470	600563	GEN-O	PROSTAGLANDIN F RECEPTOR	2244	2007A>G	3
L24470	L24470	600563	GEN-O	PROSTAGLANDIN F RECEPTOR	2299	2062A>G	3
OPRM1	L25119	600018	GEN- 4EP	Human Mu opiate receptor (MOR1) mRNA, complete cds	41	(-172)G>T	5
OPRM1	L25119	600018	GEN- 4EP	Human Mu opiate receptor (MOR1) mRNA, complete cds	102	(-111)C>T	5
OPRM1	L25119	600018	GEN- 4EP	Human Mu opiate receptor (MOR1) mRNA, complete cds	229	17C>T	A6V
OPRM1	L25119	600018	GEN- 4EP	Human Mu opiate receptor (MOR1) mRNA, complete cds	229	17C>T	A6V
OPRM1	L25119	600018	GEN- 4EP	Human Mu opiate receptor (MOR1) mRNA, complete cds	236	24G>A	S
OPRM1	L25119	600018	GEN- 4EP	Human Mu opiate receptor (MOR1) mRNA, complete cds	330	118A>G	N40D
OPRM1	L25119	600018	GEN- 4EP	Human Mu opiate receptor (MOR1) mRNA, complete cds	330	118A>G	N40D
OPRM1	L25119	600018	GEN- 4EP	Human Mu opiate receptor (MOR1) mRNA, complete cds	991	779G>A	R260H
OPRM1	L25119	600018	GEN- 4EP	Human Mu opiate receptor (MOR1) mRNA, complete cds	1005	793C>T	R265C

OPRM1	L25119	600018	GEN-4EP	Human Mu opiate receptor (MOR1) mRNA, complete cds	1154	942G>A	S
OPRM1	L25119	600018	GEN-4EP	Human Mu opiate receptor (MOR1) mRNA, complete cds	1154	942G>A	S
L25259	L25259	601020	GEN-298	Human CTLA4 counter-receptor (B7-2) mRNA, complete cds	1034	928G>A	A310T
PTGER2	L28175	601586	GEN-7C	Prostaglandin E receptor 2 (subtype EP2), 53kD	547	159C>T	S
PTGER2	L28175	601586	GEN-7C	Prostaglandin E receptor 2 (subtype EP2), 53kD	611	223G>A	V75M
PTGER2	L28175	601586	GEN-7C	Prostaglandin E receptor 2 (subtype EP2), 53kD	1725	1337A>G	Q446R
L31584	L31584	600242	GEN-MDW	Human G protein-coupled receptor (EBI 1) gene	608	545T>G	I182S
L31773	L31773	104220	GEN-4DD	Adrenergic receptor alpha 1b	171	171C>T	S
L31773	L31773	104220	GEN-4DD	Adrenergic receptor alpha 1b	534	534C>T	S
L31773	L31773	104220	GEN-4DD	Adrenergic receptor alpha 1b	549	549G>A	S
NRAMP1	L32185	600266	GEN-21Y	Homo sapiens integral membrane protein (NRAMP1) mRNA, complete cds	1399	1323C>T	S
L33798	L33798	114208	GEN-Q	Ca Channel alpha1s L-Type	5667	5442C>G	S
L33798	L33798	114208	GEN-Q	Ca Channel alpha1s L-Type	5669	5444G>C	G1815A
L33798	L33798	114208	GEN-Q	Ca Channel alpha1s L-Type	5745	5520C>G	D1840E
L33798	L33798	114208	GEN-Q	Ca Channel alpha1s L-Type	5941	5716C>A	3
L33798	L33798	114208	GEN-Q	Ca Channel alpha1s L-Type	5971	5746C>A	3
L33798	L33798	114208	GEN-Q	Ca Channel alpha1s L-Type	5985	5760G>A	3
L36719	L36719	602315	GEN-2NE	Homo sapiens MAP kinase 3 (MKK3) mRNA,	1227	890C>A	T297N

L36719	L36719	602315	GEN-2NE	Homo sapiens MAP kinase kinase 3 (MKK3) mRNA, complete cds	1271	934A>G	K312E
NRAMP2	L37347	600523	GEN-206	Human integral membrane protein (Nramp2) mRNA, complete cds	1092	1083C>T	S
ALCAM	L38608	601662	GEN-2PJ	Homo sapiens CD6 ligand (ALCAM) mRNA, complete cds	1401	1338G>A	S
L38928	L38928	None	GEN-2PT	Homo sapiens 5,10-methylenetetrahydrofolate synthetase mRNA, complete cds	617	604A>G	T202A
L40992	L40992	600211	GEN-2SO	Homo sapiens (clone PEBP2aA1) core-binding factor, runt domain, alpha subunit 1 (CBFA1) mRNA, 3 end of cds	265	265G>A	V89I
L76191	L76191	601108	GEN-3OQ	Homo sapiens interleukin-1 receptor-associated kinase (IRAK) mRNA, complete cds	902	823G>T	A275S
L76191	L76191	601108	GEN-3OQ	Homo sapiens interleukin-1 receptor-associated kinase (IRAK) mRNA, complete cds	1051	972G>A	S
L76191	L76191	601108	GEN-3OQ	Homo sapiens interleukin-1 receptor-associated kinase (IRAK) mRNA, complete cds	2191	2112C>T	S
M10901	M10901	138040	GEN-2W	Corticosteroid nuclear receptor b	1220	1088A>G	N363S
M10901	M10901	138040	GEN-2W	Corticosteroid nuclear receptor b	2024	1892-1893AG>AG	S
M10901	M10901	138040	GEN-2W	Corticosteroid nuclear receptor b	2024	1892-1893delAG	F
M10901	M10901	138040	GEN-2W	Corticosteroid nuclear receptor b	2054	1922A>T	D641V
M10901	M10901	138040	GEN-2W	Corticosteroid nuclear receptor b	2372	2240T>G	I747S

SD-144146.1

M10901	M10901	138040	GEN-2W	Corticosteroid nuclear receptor b	2391	2259A>C	L753F
M10901	M10901	138040	GEN-2W	Corticosteroid nuclear receptor b	2391	2259A>T	L753F
M11050	M11050	138040	GEN-7Y	Glucocorticoid receptor	2166	2034C>T	S
M11050	M11050	138040	GEN-7Y	Glucocorticoid receptor	3353	3221T>G	3
M11050	M11050	138040	GEN-7Y	Glucocorticoid receptor	3398	3266T>G	3
M11313	M11313	103950	GEN-E7	alpha-2-macroglobulin	1573	1530T>A	S
M11313	M11313	103950	GEN-E7	alpha-2-macroglobulin	1799	1756C>T	F
M11313	M11313	103950	GEN-E7	alpha-2-macroglobulin	3041	2998G>A	V1000I
M11313	M11313	103950	GEN-E7	alpha-2-macroglobulin	4474	4431A>C	3
M12807	M12807	186940	GEN-QG	Human T-cell surface glycoprotein T4 mRNA, complete cds	868	793C>T	R265W
M12824	M12824	186910	GEN-QH	Human T-cell differentiation antigen Leu-2/T8 mRNA, partial cds	1545	1458C>T	3
M12824	M12824	186910	GEN-QH	Human T-cell differentiation antigen Leu-2/T8 mRNA, partial cds	1765	1678C>T	3
M12959	M12959	186880	GEN-S	CD3 glycoprotein on T lymphocytes	431	295T>G	S99A
M12959	M12959	186880	GEN-S	CD3 glycoprotein on T lymphocytes	1060	924T>C	3
M12959	M12959	186880	GEN-S	CD3 glycoprotein on T lymphocytes	1129	993C>A	3
M12959	M12959	186880	GEN-S	CD3 glycoprotein on T lymphocytes	1343	1207T>C	3
M12959	M12959	186880	GEN-S	CD3 glycoprotein on T lymphocytes	1345	1209G>C	3
M12959	M12959	186880	GEN-S	CD3 glycoprotein on T lymphocytes	1394	1258T>G	3
M12959	M12959	186880	GEN-S	CD3 glycoprotein on T lymphocytes	1463	1327G>A	3
C1NH	M13690	106100	GEN-1P6	Human plasma protease (C1) inhibitor mRNA, complete cds	1475	1438G>A	V480M
C1NH	M13690	106100	GEN-1P6	Human plasma protease (C1) inhibitor mRNA, complete cds	1595	1558C>T	3

C1NH	M13690	106100	GEN-1P6	Human plasma protease (C1) inhibitor mRNA, complete cds	1714	1677A>C	3
BCL2	M13994	151430	GEN-1Q9	Human B-cell leukemia/lymphoma 2 (bcl-2) proto-oncogene mRNA encoding bcl-2-alpha protein, complete cds	1744	286G>A	A96T
BCL2	M13994	151430	GEN-1Q9	Human B-cell leukemia/lymphoma 2 (bcl-2) proto-oncogene mRNA encoding bcl-2-alpha protein, complete cds	1786	328G>C	G110R
BCL2	M13994	151430	GEN-1Q9	Human B-cell leukemia/lymphoma 2 (bcl-2) proto-oncogene mRNA encoding bcl-2-alpha protein, complete cds	2959	1501A>G	3
C1R	M14058	216950	GEN-1QJ	Human complement C1r mRNA, complete cds	1519	1456C>T	R486C
ARG1	M14502	207800	GEN-1RE	Human liver arginase mRNA, complete cds	800	744C>T	S
NGFR	M14764	162010	GEN-1S8	Human nerve growth factor receptor mRNA, complete cds	2716	2603C>T	3
NGFR	M14764	162010	GEN-1S8	Human nerve growth factor receptor mRNA, complete cds	2729	2616C>T	3
NGFR	M14764	162010	GEN-1S8	Human nerve growth factor receptor mRNA, complete cds	2912	2799G>A	3
NGFR	M14764	162010	GEN-1S8	Human nerve growth factor receptor mRNA, complete cds	3252	3139C>G	3
M14766	M14766	151445	GEN-QQ	Human Fc-epsilon receptor CD23 antigen (IgE receptor) mRNA complete cds	1338	1153G>A	3
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	466	(-1122)C>G	5
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	565	(-1023)G>A	5
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	1182	(-406)C>T	5

M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	1221	(-367)C>T	5
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	1326	(-262)G>A	5
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	1541	(-47)C>T	5
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	1633	46A>G	R16G
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	1633	46A>G	R16G
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	1666	79C>G	Q27E
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	1666	79C>G	Q27E
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	1666	79C>G	Q27E
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	1687	100G>A	V34M
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	1839	252G>A	S
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	2110	523C>A	S
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	2640	1053G>C	S
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	2826	1239G>A	S
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	2862	1275C>G	3
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	2864	1277C>A	3
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	2865	1278C>A	3
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	3371	1784A>T	3
M15395	M15395	600065	GEN-U	Leukocyte integrin beta-2	890	818G>A	G273E
M15395	M15395	600065	GEN-U	Leukocyte integrin beta-2	978	906A>G	S
M15395	M15395	600065	GEN-U	Leukocyte integrin beta-2	1173	1101C>A	S
M15395	M15395	600065	GEN-U	Leukocyte integrin beta-2	1395	1323T>C	S
M15395	M15395	600065	GEN-U	Leukocyte integrin beta-2	1614	1542C>T	S
M15395	M15395	600065	GEN-U	Leukocyte integrin beta-2	1965	1893C>T	S
M15395	M15395	600065	GEN-U	Leukocyte integrin beta-2	2505	2433G>A	3
M15395	M15395	600065	GEN-U	Leukocyte integrin beta-2	2505	2433G>A	3
M15395	M15395	600065	GEN-U	Leukocyte integrin beta-2	2528	2456C>A	3
M15395	M15395	600065	GEN-U	Leukocyte integrin beta-2	2528	2456C>A	3
M15395	M15395	600065	GEN-U	Leukocyte integrin beta-2	2553	2481G>C	3
M15395	M15395	600065	GEN-U	Leukocyte integrin beta-2	1160	1160A>C	3
DAF	M15799	125240	GEN-1UD	Human complement decay-accelerating factor (DAF) mRNA; 3 end			
M16405	M16405	None	GEN-4ES	Muscarinic receptor, CHRM4	2138	1338C>T	S
M16405	M16405	None	GEN-4ES	Muscarinic receptor, CHRM4	2409	1609G>A	3
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	422	293A>G	D98G

M16541	M16541	177400	GEN-35	Butyrylcholinesterase	557	428G>A	G143D
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	564	435- 436TT>AG>A	F146V
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	568	G 439C>T	F
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	596	467A>G	Y156C
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	941	812C>T	T271M
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	961	832A>C	T278P
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	978	849G>C	E283D
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1201	1072T>A	L358I
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1306	1177G>A	G393R
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1382	1253G>T	G418V
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1549	1420T>G	F474V
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1564	1435G>T	F
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1703	1574A>T	E525V
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1756	1627C>T	R543C
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1828	1699G>A	A567T
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1828	1699G>A	A567T
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	2127	1998A>G	3
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	2127	1998A>G	3
M16541	M16973	120960	GEN-1ZA	Human complement protein C8 beta subunit mRNA, complete cds	1860	1833C>T	3
CYP21	M17252	201910	GEN-201	Human cytochrome P450c21 mRNA, 3 end	224	224G>A	R75H
CYP21	M17252	201910	GEN-201	Human cytochrome P450c21 mRNA, 3 end	330	330C>T	S
CYP21	M17252	201910	GEN-201	Human cytochrome P450c21 mRNA, 3 end	745	745T>C	3
C8G	M17999	120930	GEN-20Y	Human complement component C8-gamma mRNA, complete cds	193	132T>G	S
M19045	M19045	153450	GEN-QZ	Human lysozyme mRNA, complete cds	156	143G>T	C48F
M19045	M19045	153450	GEN-QZ	Human lysozyme mRNA, complete cds	638	625T>C	3
M19045	M19045	153450	GEN-QZ	Human lysozyme mRNA, complete cds	825	812A>G	3

M19045	M19045	153450	GEN-QZ	Human lysozyme mRNA, complete cds	876	863T>C	3
M19045	M19045	153450	GEN-QZ	Human lysozyme mRNA, complete cds	939	926C>T	3
M19045	M19045	153450	GEN-QZ	Human lysozyme mRNA, complete cds	973	960T>C	3
M19045	M19045	153450	GEN-QZ	Human lysozyme mRNA, complete cds	981	968A>G	3
M19045	M19045	153450	GEN-QZ	Human lysozyme mRNA, complete cds	1018	1005G>A	3
M19045	M19045	153450	GEN-QZ	Human lysozyme mRNA, complete cds	1304	1291C>T	3
M20137	M20137	147740	GEN- CCJ	Human interleukin 3 (IL-3) mRNA, complete cds, clone pcD-SR-alpha	132	79C>T	P27S
M20566	M20566	147880	GEN-3A	Interleukin 6A	3058	2621A>T	3
M21054	M21054	172410	GEN-3B	Phospholipase A-2 (PLA-2) lung	331	294G>A	S
M21054	M21054	172410	GEN-3B	Phospholipase A-2 (PLA-2) lung	400	363C>A	D121E
SCYA5	M21121	187011	GEN- 24E	Human T cell-specific protein (RANTES) mRNA, complete cds	234	208C>T	R70C
SCYA5	M21121	187011	GEN- 24E	Human T cell-specific protein (RANTES) mRNA, complete cds	524	498T>C	3
SCYA5	M21121	187011	GEN- 24E	Human T cell-specific protein (RANTES) mRNA, complete cds	634	608C>T	3
SCYA5	M21121	187011	GEN- 24E	Human T cell-specific protein (RANTES) mRNA, complete cds	666	640C>T	3
SCYA5	M21121	187011	GEN- 24E	Human T cell-specific protein (RANTES) mRNA, complete cds	667	641G>A	3
SCYA5	M21121	187011	GEN- 24E	Human T cell-specific protein (RANTES) mRNA, complete cds	690	664G>A	3
SCYA5	M21121	187011	GEN- 24E	Human T cell-specific protein (RANTES) mRNA, complete cds	695	669C>T	3

SCYA5	M21121	187011	GEN-24E	Human T cell-specific protein (RANTES) mRNA, complete cds	696	670G>A	3
SCYA5	M21121	187011	GEN-24E	Human T cell-specific protein (RANTES) mRNA, complete cds	698	672G>A	3
SCYA5	M21121	187011	GEN-24E	Human T cell-specific protein (RANTES) mRNA, complete cds	702	676C>A	3
SCYA5	M21121	187011	GEN-24E	Human T cell-specific protein (RANTES) mRNA, complete cds	719	693C>T	3
SCYA5	M21121	187011	GEN-24E	Human T cell-specific protein (RANTES) mRNA, complete cds	728	702G>A	3
SCYA5	M21121	187011	GEN-24E	Human T cell-specific protein (RANTES) mRNA, complete cds	735	709C>T	3
SCYA5	M21121	187011	GEN-24E	Human T cell-specific protein (RANTES) mRNA, complete cds	736	710G>A	3
M22324	M22324	151530	GEN-25R	Human aminopeptidase N/CD13 mRNA encoding aminopeptidase N, complete cds	1052	932C>T	A311V
M22324	M22324	151530	GEN-25R	Human aminopeptidase N/CD13 mRNA encoding aminopeptidase N, complete cds	2168	2048C>G	T683S
M22324	M22324	151530	GEN-25R	Human aminopeptidase N/CD13 mRNA encoding aminopeptidase N, complete cds	2375	2255G>A	S752N
M22324	M22324	151530	GEN-25R	Human aminopeptidase N/CD13 mRNA encoding aminopeptidase N, complete cds	2505	2385C>T	S
M22324	M22324	151530	GEN-25R	Human aminopeptidase N/CD13 mRNA encoding aminopeptidase N, complete cds	3053	2933G>C	3

M22324	M22324	151530	GEN-25R	Human aminopeptidase N/CD13 mRNA encoding aminopeptidase N, complete cds	3299	3179A>G	3
M22324	M22324	151530	GEN-25R	Human aminopeptidase N/CD13 mRNA encoding aminopeptidase N, complete cds	3405	3285C>T	3
PLA2G2A	M22430	172411	GEN-25V	Human RASf-A PLA2 mRNA, complete cds	116	(-20)G>T	5
PLA2G2A	M22430	172411	GEN-25V	Human RASf-A PLA2 mRNA, complete cds	231	96G>C	S
PLA2G2A	M22430	172411	GEN-25V	Human RASf-A PLA2 mRNA, complete cds	267	132C>T	S
PLA2G2A	M22430	172411	GEN-25V	Human RASf-A PLA2 mRNA, complete cds	267	132C>T	S
PLA2G2A	M22430	172411	GEN-25V	Human RASf-A PLA2 mRNA, complete cds	278	143-144GT>GT	S
PLA2G2A	M22430	172411	GEN-25V	Human RASf-A PLA2 mRNA, complete cds	278	143-144delGT	F
PLA2G2A	M22430	172411	GEN-25V	Human RASf-A PLA2 mRNA, complete cds	643	508C>T	3
PLA2G2A	M22430	172411	GEN-25V	Human RASf-A PLA2 mRNA, complete cds	700	565G>C	3
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	238	167A>T	K56M
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	238	167A>T	K56M
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	792	721G>A	G241R
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	792	721G>A	G241R
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	1126	1055C>T	P352L
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	1166	1095C>T	S
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	1295	1224G>A	S
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	1476	1405A>G	K469E
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	1476	1405A>G	K469E

M24283	M24283	147840	GEN-V	molecule 1	1476	1405A>G	K469E
				Intercellular adhesion molecule 1			
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	2043	1972C>T	3
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	2043	1972C>T	3
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	2551	2480C>T	3
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	2681	2610G>A	3
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	2842	2771G>A	3
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	2842	2771G>A	3
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	2935	2864T>C	3
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	2938	2867G>A	3
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	2950	2879C>T	3
CD36	M24795	173510	GEN-28R	Human CD36 antigen mRNA, complete cds	79	(-132)C>A	5
CD36	M24795	173510	GEN-28R	Human CD36 antigen mRNA, complete cds	341	131T>G	L44R
CD36	M24795	173510	GEN-28R	Human CD36 antigen mRNA, complete cds	1851	1641A>G	3
M24857	M24857	180190	GEN-80	Retinoic acid receptor, gamma 1	1694	1280C>T	S427L
SELL	M25280	153240	GEN-29J	Human lymph node homing receptor mRNA, complete cds	436	321T>C	S
SELL	M25280	153240	GEN-29J	Human lymph node homing receptor mRNA, complete cds	692	577C>T	L193F
SELL	M25280	153240	GEN-29J	Human lymph node homing receptor mRNA, complete cds	1378	1263C>T	3
SELL	M25280	153240	GEN-29J	Human lymph node homing receptor mRNA, complete cds	2157	2042A>C	3

SELL	M25280	153240	GEN-29J	Human lymph node, homologous receptor mRNA, complete cds	2215	2100C>G	3
SCYA3	M25315	601395	GEN-29M	Homo sapiens (clone pAT 464) potential lymphokine/cytokine mRNA, complete cds	32	(-52)T>C	5
SCYA3	M25315	601395	GEN-29M	Homo sapiens (clone pAT 464) potential lymphokine/cytokine mRNA, complete cds	67	(-17)G>A	5
SCYA3	M25315	601395	GEN-29M	Homo sapiens (clone pAT 464) potential lymphokine/cytokine mRNA, complete cds	110	27T>C	S
SCYA3	M25315	601395	GEN-29M	Homo sapiens (clone pAT 464) potential lymphokine/cytokine mRNA, complete cds	153	70T>C	S24P
SCYA3	M25315	601395	GEN-29M	Homo sapiens (clone pAT 464) potential lymphokine/cytokine mRNA, complete cds	203	120G>A	S
SCYA3	M25315	601395	GEN-29M	Homo sapiens (clone pAT 464) potential lymphokine/cytokine mRNA, complete cds	263	180C>T	S
SCYA3	M25315	601395	GEN-29M	Homo sapiens (clone pAT 464) potential lymphokine/cytokine mRNA, complete cds	264	181G>A	G61S
SCYA3	M25315	601395	GEN-29M	Homo sapiens (clone pAT 464) potential lymphokine/cytokine mRNA, complete cds	285	202C>A	S
SCYA3	M25315	601395	GEN-29M	Homo sapiens (clone pAT 464) potential lymphokine/cytokine mRNA, complete cds	288	205A>G	S69G
SCYA3	M25315	601395	GEN-29M	Homo sapiens (clone pAT 464) potential lymphokine/cytokine mRNA, complete cds	291	208C>G	R70G

SCYA3	M25315	601395	GEN- 29M	lymphokine/cytokine mRNA, complete cds Homo sapiens (clone pAT 464) potential	335	252T>C	S
SCYA3	M25315	601395	GEN- 29M	lymphokine/cytokine mRNA, complete cds Homo sapiens (clone pAT 464) potential	341	258C>T	S
SCYA3	M25315	601395	GEN- 29M	lymphokine/cytokine mRNA, complete cds Homo sapiens (clone pAT 464) potential	395	312G>A	3
SCYA3	M25315	601395	GEN- 29M	lymphokine/cytokine mRNA, complete cds Homo sapiens (clone pAT 464) potential	452	369C>T	3
SCYA3	M25315	601395	GEN- 29M	lymphokine/cytokine mRNA, complete cds Homo sapiens (clone pAT 464) potential	479	396G>A	3
SCYA3	M25315	601395	GEN- 29M	lymphokine/cytokine mRNA, complete cds Homo sapiens (clone pAT 464) potential	549	466G>A	3
SCYA3	M25315	601395	GEN- 29M	lymphokine/cytokine mRNA, complete cds Homo sapiens (clone pAT 464) potential	561	478C>T	3
SCYA3	M25315	601395	GEN- 29M	lymphokine/cytokine mRNA, complete cds Homo sapiens (clone pAT 464) potential	617	534C>G	3
SCYA3	M25315	601395	GEN- 29M	lymphokine/cytokine mRNA, complete cds Homo sapiens (clone pAT 464) potential	660	577A>G	3
M25813	M25813	None	GEN- 2A0	lymphokine/cytokine mRNA, complete cds Human unidentified gene complementary to P450c21 gene, partial cds	1357	1357G>A	V453I

M25813	M25813	None	GEN-2A0	Human unidentified gene complementary to P450c21 gene, partial cds	2082	2082C>G	I694M
M25813	M25813	None	GEN-2A0	Human unidentified gene complementary to P450c21 gene, partial cds	2502	2502G>A	3
M25813	M25813	None	GEN-2A0	Human unidentified gene complementary to P450c21 gene, partial cds	2626	2626A>G	3
M26383	M26383	146930	GEN-3E	Interleukin 8	259	185C>G	A62G
M26383	M26383	146930	GEN-3E	Interleukin 8	1237	1163A>T	3
M26383	M26383	146930	GEN-3E	Interleukin 8	1281	1207A>G	3
M27492	M27492	147810	GEN-3F	INTERLEUKIN 1 RECEPTOR, TYPE I	4686	4604T>G	3
M28226	M28226	158105	GEN-R8	Human JE gene encoding a monocyte secretory protein mRNA, complete cds	90	44C>G	A15G
M28226	M28226	158105	GEN-R8	Human JE gene encoding a monocyte secretory protein mRNA, complete cds	151	105C>T	S
M28226	M28226	158105	GEN-R8	Human JE gene encoding a monocyte secretory protein mRNA, complete cds	411	365T>C	3
POMC	M28636	176830	GEN-2DG	Adrenocorticotrophic hormone (ACTH)	92	92C>T	3
CFTR	M28668	602421	GEN-2DF	Human cystic fibrosis mRNA, encoding a presumed transmembrane conductance regulator (CFTR)	2729	2597G>A	C866Y
CFTR	M28668	602421	GEN-2DF	Human cystic fibrosis mRNA, encoding a presumed transmembrane conductance regulator (CFTR)	5826	5694T>C	3
CD1B	M28826	188360	GEN-2DO	Human thymocyte antigen CD1b mRNA, complete cds	886	841G>A	V281M

M29551	M29551	114106	GEN-F3	SERINE/THREONINE PROTEIN PHOSPHATASE 2B CATALYTIC SUBUNIT, BETA ISOFORM	936	820G>A	V274M
M29551	M29551	114106	GEN-F3	SERINE/THREONINE PROTEIN PHOSPHATASE 2B CATALYTIC SUBUNIT, BETA ISOFORM	2640	2524G>A	3
M29696	M29696	146661	GEN-3H	Interleukin 7 receptor	1088	1066G>A	V356I
M30640	M30640	131210	GEN-RB	Human endothelial leukocyte adhesion molecule 1 (ELAM1) mRNA, complete cds	3506	3366A>G	3
M30773	M30773	114106	GEN-X	Calcineurin B type I	331	(-428)T>C	5
M30773	M30773	114106	GEN-X	Calcineurin B type I	1658	900C>A	3
M30938	M30938	194364	GEN-F5	ATP-DEPENDENT DNA HELICASE II, 86 KD SUBUNIT	1599	1572A>G	S
M30938	M30938	194364	GEN-F5	ATP-DEPENDENT DNA HELICASE II, 86 KD SUBUNIT	2549	2522T>C	3
M30938	M30938	194364	GEN-F5	ATP-DEPENDENT DNA HELICASE II, 86 KD SUBUNIT	2953	2926C>A	3
M30938	M30938	194364	GEN-F5	ATP-DEPENDENT DNA HELICASE II, 86 KD SUBUNIT	2953	2926C>A	3
M30938	M30938	194364	GEN-F5	ATP-DEPENDENT DNA HELICASE II, 86 KD SUBUNIT	3037	3010G>A	3
M30938	M30938	194364	GEN-F5	ATP-DEPENDENT DNA HELICASE II, 86 KD SUBUNIT	3067	3040G>A	3
M31523	M31523	147141	GEN-F7	Transcription factor 3 (E2A immunoglobulin enhancer binding factors E12/E47) SUBUNIT	1321	1291G>A	G431S
M31523	M31523	147141	GEN-F7	Transcription factor 3 (E2A immunoglobulin enhancer binding factors E12/E47) SUBUNIT	1323	1293C>T	S

M31523	M31523	147141	GEN-F7	binding factors E12/E47) Transcription factor 3 (E2A immunoglobulin enhancer binding factors E12/E47)	1332	1302G>A	S
M31523	M31523	147141	GEN-F7	Transcription factor 3 (E2A immunoglobulin enhancer binding factors E12/E47)	1338	1308T>C	S
M31523	M31523	147141	GEN-F7	Transcription factor 3 (E2A immunoglobulin enhancer binding factors E12/E47)	1608	1578C>G	S
M31523	M31523	147141	GEN-F7	Transcription factor 3 (E2A immunoglobulin enhancer binding factors E12/E47)	4022	3992G>A	3
M31523	M31523	147141	GEN-F7	Transcription factor 3 (E2A immunoglobulin enhancer binding factors E12/E47)	4254	4224T>A	3
M32315	M32315	191191	GEN-3M	binding factors E12/E47) Tumor necrosis factor receptor 2 (75kD)	676	587T>G	M196R
M32315	M32315	191191	GEN-3M	Tumor necrosis factor receptor 2 (75kD)	1176	1087G>A	A363T
M32315	M32315	191191	GEN-3M	Tumor necrosis factor receptor 2 (75kD)	1668	1579G>T	3
M32315	M32315	191191	GEN-3M	Tumor necrosis factor receptor 2 (75kD)	2898	2809G>A	3
M32315	M32315	191191	GEN-3M	Tumor necrosis factor receptor 2 (75kD)	3671	3582G>A	3
VEGF	M32977	192240	GEN-2JF	receptor 2 (75kD) Human heparin-binding vascular endothelial growth factor (VEGF) mRNA, complete cds	50	(-7)C>T	5
VEGF	M32977	192240	GEN-2JF	Human heparin-binding vascular endothelial growth factor (VEGF) mRNA, complete cds	92	36C>T	S
M33195	M33195	147139	GEN-2JR	Human Fc-epsilon-receptor gamma-chain mRNA, complete cds	446	421T>G	3
M33195	M33195	147139	GEN-2JR	Human Fc-epsilon-receptor gamma-chain mRNA, complete cds	489	464T>C	3
M33491	M33491	191080	GEN-RD	Human tryptase-I mRNA, 3	92	92C>T	S31L

M33491	M33491	191080	GEN-RD	Human tryptase-I mRNA, 3 end	392	392C>G	T131R
M33491	M33491	191080	GEN-RD	Human tryptase-I mRNA, 3 end	609	609G>A	S
M33491	M33491	191080	GEN-RD	Human tryptase-I mRNA, 3 end	707	707G>A	C236Y
M33491	M33491	191080	GEN-RD	Human tryptase-I mRNA, 3 end	730	730G>A	A244T
M33491	M33491	191080	GEN-RD	Human tryptase-I mRNA, 3 end	837	837T>G	3
M33491	M33491	191080	GEN-RD	Human tryptase-I mRNA, 3 end	840	840G>T	3
M33491	M33491	191080	GEN-RD	Human tryptase-I mRNA, 3 end	1008	1008T>C	3
M33491	M33491	191080	GEN-RD	Human tryptase-I mRNA, 3 end	1050	1050C>T	3
M33491	M33491	191080	GEN-RD	Human tryptase-I mRNA, 3 end	1060	1060A>G	3
M33680	M33680	186845	GEN- 2K3	Human 26-kDa cell surface protein TAPA-1 mRNA, complete cds	1065	827G>A	3
M33680	M33680	186845	GEN- 2K3	Human 26-kDa cell surface protein TAPA-1 mRNA, complete cds	1284	1046T>C	3
M33680	M33680	186845	GEN- 2K3	Human 26-kDa cell surface protein TAPA-1 mRNA, complete cds	1412	1174C>T	3
M33680	M33680	186845	GEN- 2K3	Human 26-kDa cell surface protein TAPA-1 mRNA, complete cds	1416	1178G>A	3
HLA- DQB1	M33907	142857	GEN- 2KB	Human MHC class II HLA- DQB1 mRNA, complete cds	561	516T>C	S
HLA- DQB1	M33907	142857	GEN- 2KB	Human MHC class II HLA- DQB1 mRNA, complete cds	641	596G>A	R199H
HLA- DQB1	M33907	142857	GEN- 2KB	Human MHC class II HLA- DQB1 mRNA, complete cds	648	603C>T	S
HLA- DQB1	M33907	142857	GEN- 2KB	Human MHC class II HLA- DQB1 mRNA, complete cds	695	650T>C	I217T

DQB1	2KB	DQB1 mRNA, complete cds			
HLA-DQB1	GEN-2KB	Human MHC class II HLA-DQB1 mRNA, complete cds	771	726G>C	S
HLA-DQB1	GEN-2KB	Human MHC class II HLA-DQB1 mRNA, complete cds	780	735C>T	S
M34539	GEN-3N	FKBP, tacrolimus binding protein, FK506-binding protein 1 (12kD)	449	371A>G	3
M34539	GEN-3N	FKBP, tacrolimus binding protein, FK506-binding protein 1 (12kD)	486	408G>A	3
M34539	GEN-3N	FKBP, tacrolimus binding protein, FK506-binding protein 1 (12kD)	650	572T>C	3
M35011	GEN-2LV	Human integrin beta-5 subunit mRNA, complete cds	1448	1419C>T	S
M35011	GEN-2LV	Human integrin beta-5 subunit mRNA, complete cds	2778	2749A>C	3
M35011	GEN-2LV	Human integrin beta-5 subunit mRNA, complete cds	2904	2875T>C	3
M35011	GEN-2LV	Human integrin beta-5 subunit mRNA, complete cds	3077	3048G>A	3
M35011	GEN-2LV	Human integrin beta-5 subunit mRNA, complete cds	3095	3066T>A	3
M35999	GEN-Y	Leukocyte integrin beta-3	53	35T>C	V12A
M35999	GEN-Y	Leukocyte integrin beta-3	149	131C>A	A44D
M35999	GEN-Y	Leukocyte integrin beta-3	194	176T>C	L59P
M35999	GEN-Y	Leukocyte integrin beta-3	364	346C>T	L116F
M35999	GEN-Y	Leukocyte integrin beta-3	900	882T>C	S
M35999	GEN-Y	Leukocyte integrin beta-3	987	969G>T	E323D
M35999	GEN-Y	Leukocyte integrin beta-3	1161	1143C>A	S
M35999	GEN-Y	Leukocyte integrin beta-3	1161	1143C>A	S

M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	1551	1533G>A	S
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	1551	1533G>A	S
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	1562	1544G>A	R515Q
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	1563	1545G>A	S
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	1563	1545G>A	S
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	2226	2208C>T	S
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	2426	2408G>C	3
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	3056	3038C>T	3
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	3098	3080A>G	3
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	3403	3385A>T	3
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	3927	3909C>T	3
LIG1	M36067	126391	GEN-2MS	Human DNA ligase I mRNA, complete cds	2526	2406T>C	S
M36712	M36712	186730	GEN-2NC	Human T lymphocyte surface glycoprotein (CD8-beta) mRNA, complete cds	1046	1001C>A	3
M36712	M36712	186730	GEN-2NC	Human T lymphocyte surface glycoprotein (CD8-beta) mRNA, complete cds	1281	1236T>C	3
M36712	M36712	186730	GEN-2NC	Human T lymphocyte surface glycoprotein (CD8-beta) mRNA, complete cds	1326	1281C>A	3
PLCG2	M37238	600220	GEN-2O1	Phospholipase C gamma-2	449	297A>G	S
PLCG2	M37238	600220	GEN-2O1	Phospholipase C gamma-2	883	731A>G	H244R
PLCG2	M37238	600220	GEN-2O1	Phospholipase C gamma-2	922	770A>T	H257L
PLCG2	M37238	600220	GEN-2O1	Phospholipase C gamma-2	954	802C>T	R268W
PLCG2	M37238	600220	GEN-2O1	Phospholipase C gamma-2	1301	1149T>C	S
PLCG2	M37238	600220	GEN-2O1	Phospholipase C gamma-2	1649	1497T>C	S
PLCG2	M37238	600220	GEN-2O1	Phospholipase C gamma-2	2666	2514G>A	S
PLCG2	M37238	600220	GEN-2O1	Phospholipase C gamma-2	3245	3093C>T	S
PLCG2	M37238	600220	GEN-2O1	Phospholipase C gamma-2	3245	3093C>T	S

PLCG2	M37238	600220	201	GEN-201	Phospholipase C gamma-2	3436	3284G>A	G1095D
PLCG2	M37238	600220	201	GEN-201	Phospholipase C gamma-2	4207	4055C>G	3
PECAM1	M37780	173445	201	GEN-201	Human leukocyte surface protein (CD31) mRNA, complete cds	152	27C>G	S
PECAM1	M37780	173445	201	GEN-201	Human leukocyte surface protein (CD31) mRNA, complete cds	1577	1452C>T	S
PECAM1	M37780	173445	201	GEN-201	Human leukocyte surface protein (CD31) mRNA, complete cds	1813	1688A>G	N563S
PECAM1	M37780	173445	201	GEN-201	Human leukocyte surface protein (CD31) mRNA, complete cds	2133	2008G>A	G670R
PECAM1	M37780	173445	201	GEN-201	Human leukocyte surface protein (CD31) mRNA, complete cds	2400	2275G>A	3
CD9	M38690	143030	201	GEN-201	Human CD9 antigen mRNA, complete cds	819	768T>G	3
CD9	M38690	143030	201	GEN-201	Human CD9 antigen mRNA, complete cds	826	775T>G	3
CD9	M38690	143030	201	GEN-201	Human CD9 antigen mRNA, complete cds	947	896G>A	3
M55040	M55040	100740	201	GEN-201	acetylcholinesterase	323	167C>T	P56L
M55040	M55040	100740	201	GEN-201	acetylcholinesterase	1154	998T>A	V333E
M55040	M55040	100740	201	GEN-201	acetylcholinesterase	1213	1057C>A	H353N
M55040	M55040	100740	201	GEN-201	acetylcholinesterase	1482	1326G>T	S
M55040	M55040	100740	201	GEN-201	acetylcholinesterase	1587	1431C>T	S
M55040	M55040	100740	201	GEN-201	acetylcholinesterase	1587	1431C>T	S
M55040	M55040	100740	201	GEN-201	acetylcholinesterase	1663	1507T>C	F503L
CSNK2A1	M55265	115440	201	GEN-201	Human casein kinase II alpha subunit mRNA, complete cds	193	45T>C	S
CSNK2A1	M55265	115440	201	GEN-201	Human casein kinase II alpha subunit mRNA, complete cds	1007	859A>C	S287R
CSNK2A1	M55265	115440	201	GEN-201	Human casein kinase II alpha subunit mRNA, complete cds	1180	1032G>A	S

CSNK2A1	M55265	115440	35Y GEN-35Y	alpha subunit mRNA, complete cds	1199	1051A>G	M351V
CSNK2A2	M55268	115442	GEN-35X	Human casein kinase II alpha subunit mRNA, complete cds	1532	1369C>A	3
M55643	M55643	164011	GEN-RP	Human casein kinase II alpha subunit mRNA, complete cds	1936	1755G>A	S
M57414	M57414	None	GEN-4FK	Human factor KBF1 mRNA, complete cds	68	68T>C	I23T
M57414	M57414	None	GEN-4FK	Human neurokinin A receptor (NK-2R) mRNA, complete cds	951	951G>A	S
M57414	M57414	None	GEN-4FK	Human neurokinin A receptor (NK-2R) mRNA, complete cds	1171	1171C>G	P391A
M58525	M58525	116790	GEN-3S	complete cds	390	186T>C	S
M58525	M58525	116790	GEN-3S	Catechol-O- methyltransferase	390	186T>C	S
M58525	M58525	116790	GEN-3S	Catechol-O- methyltransferase	418	214G>T	A72S
M58525	M58525	116790	GEN-3S	Catechol-O- methyltransferase	423	219G>A	S
M58525	M58525	116790	GEN-3S	Catechol-O- methyltransferase	612	408C>G	S
M58525	M58525	116790	GEN-3S	Catechol-O- methyltransferase	676	472A>G	M158V
M58525	M58525	116790	GEN-3S	Catechol-O- methyltransferase	676	472A>G	M158V
M58525	M58525	116790	GEN-3S	Catechol-O- methyltransferase	813	609C>T	S
M58525	M58525	116790	GEN-3S	Catechol-O- methyltransferase	1031	827delC	F
M58525	M58525	116790	GEN-3S	Catechol-O- methyltransferase	1039	835C>A	3
M58664	M58664	103000	GEN-395	methylyltransferase Homo sapiens CD24 signal transducer mRNA,	226	170C>T	A57V

M58664	M58664	103000	GEN-395	Homo sapiens CD24 signal transducer mRNA, complete cds	570	514A>T	3
M58664	M58664	103000	GEN-395	Homo sapiens CD24 signal transducer mRNA, complete cds	1109	1053A>G	3
M58664	M58664	103000	GEN-395	Homo sapiens CD24 signal transducer mRNA, complete cds	1334	1278C>G	3
M58664	M58664	103000	GEN-395	Homo sapiens CD24 signal transducer mRNA, complete cds	1345	1289T>C	3
M58664	M58664	103000	GEN-395	Homo sapiens CD24 signal transducer mRNA, complete cds	1374	1318C>T	3
M58664	M58664	103000	GEN-395	Homo sapiens CD24 signal transducer mRNA, complete cds	1403	1347C>T	3
M58664	M58664	103000	GEN-395	Homo sapiens CD24 signal transducer mRNA, complete cds	1408	1352T>G	3
M58664	M58664	103000	GEN-395	Homo sapiens CD24 signal transducer mRNA, complete cds	1415	1359C>A	3
M58664	M58664	103000	GEN-395	Homo sapiens CD24 signal transducer mRNA, complete cds	1677	1621A>G	3
CD48	M59904	109530	GEN-3AE	Human pan-leukocyte antigen (CD48) mRNA, complete cds	903	886T>G	3
M59979	M59979	176805	GEN-Z	Cyclooxygenase 1 COX1	644	639C>A	S
M59979	M59979	176805	GEN-Z	Cyclooxygenase 1 COX1	1892	1887C>A	3
M59979	M59979	176805	GEN-Z	Cyclooxygenase 1 COX1	2030	2025G>A	3
M60335	M60335	192225	GEN-3U	Vascular cell adhesion molecule 1	1562	1463A>G	H488R
M60335	M60335	192225	GEN-3U	Vascular cell adhesion molecule 1	2178	2079C>T	S
M60335	M60335	192225	GEN-3U	Vascular cell adhesion molecule 1	2178	2079C>T	S

M60335	M60335	192225	GEN-3U	Vascular cell adhesion molecule 1	2196	2097T>C	S
M60335	M60335	192225	GEN-3U	Vascular cell adhesion molecule 1	2307	2208A>G	S
M60335	M60335	192225	GEN-3U	Vascular cell adhesion molecule 1	2321	2222T>C	3
TCN2	M60396	275350	GEN-3AX	Human transcobalamin II (TCII) mRNA, complete cds	1164	1127C>T	S376L
TCN2	M60396	275350	GEN-3AX	Human transcobalamin II (TCII) mRNA, complete cds	1765	1728T>C	3
FPR1	M60626	136537	GEN-3B5	Human N-formylpeptide receptor (fMLP-R98) mRNA, complete cds	1082	1037C>A	A346E
FPR1	M60626	136537	GEN-3B5	Human N-formylpeptide receptor (fMLP-R98) mRNA, complete cds	1164	1119G>C	3
M60857	M60857	123841	GEN-10	Cyclophilin B	183	171C>T	S
M60857	M60857	123841	GEN-10	Cyclophilin B	217	205G>T	V69L
M60857	M60857	123841	GEN-10	Cyclophilin B	702	690C>T	3
M60857	M60857	123841	GEN-10	Cyclophilin B	804	792A>C	3
CD53	M60871	151525	GEN-3BA	Human cell surface antigen (CD53) mRNA, complete cds	645	572G>A	C191Y
M61764	M61764	191135	GEN-FO	Tubulin, gamma polypeptide	693	669A>G	S
M61764	M61764	191135	GEN-FO	Tubulin, gamma polypeptide	723	699T>C	S
M61764	M61764	191135	GEN-FO	Tubulin, gamma polypeptide	849	825T>G	S
M61764	M61764	191135	GEN-FO	Tubulin, gamma polypeptide	858	834G>A	S
M61764	M61764	191135	GEN-FO	Tubulin, gamma polypeptide	1033	1009T>C	S
M61764	M61764	191135	GEN-FO	Tubulin, gamma polypeptide	1053	1029C>G	S
M61764	M61764	191135	GEN-FO	Tubulin, gamma polypeptide	1131	1107G>A	S
M61764	M61764	191135	GEN-FO	Tubulin, gamma polypeptide	1188	1164C>T	S

M64592	M64592	120420	GEN-3X	Granulocyte colony-stimulating factor	271	271T>G	Y91D
M64592	M64592	120420	GEN-3X	Granulocyte colony-stimulating factor	1533	1533C>T	S
M64799	M64799	None	GEN-4DN	Histamine receptor H2	398	398T>C	V133A
M64799	M64799	None	GEN-4DN	Histamine receptor H2	525	525A>T	K175N
M64799	M64799	None	GEN-4DN	Histamine receptor H2	620	620A>G	K207R
M64799	M64799	None	GEN-4DN	Histamine receptor H2	649	649A>G	N217D
M64799	M64799	None	GEN-4DN	Histamine receptor H2	692	692A>G	K231R
M64799	M64799	None	GEN-4DN	Histamine receptor H2	802	802G>A	V268M
C5	M65134	120900	GEN-3FT	Human complement component C5 mRNA, 3'end	1171	1171A>G	I391V
EDN2	M65199	131241	GEN-CBS	Endothelin 2	384	314C>T	A105V
EDN2	M65199	131241	GEN-CBS	Endothelin 2	997	927A>G	3
EDN2	M65199	131241	GEN-CBS	Endothelin 2	997	927A>G	3
M67439	M67439	126453	GEN-4EI	Dopamine Receptor D5	1500	1353T>A	S
M67439	M67439	126453	GEN-4EI	Dopamine Receptor D5	1512	1365G>A	F
M67439	M67439	126453	GEN-4EI	Dopamine Receptor D5	1566	1419G>A	S
M68892	M68892	147559	GEN-15	Leukocyte integrin beta-7	1327	1176C>T	S
M69043	M69043	164008	GEN-3IZ	Homo sapiens MAD-3 mRNA encoding IκB-like activity, complete cds	400	306T>C	S
M69043	M69043	164008	GEN-3IZ	Homo sapiens MAD-3 mRNA encoding IκB-like activity, complete cds	1050	956T>C	3
M69043	M69043	164008	GEN-3IZ	Homo sapiens MAD-3 mRNA encoding IκB-like activity, complete cds	1119	1025G>A	3
M69043	M69043	164008	GEN-3IZ	Homo sapiens MAD-3 mRNA encoding IκB-like activity, complete cds	1174	1080A>G	3

M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	435	385A>C	S
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	936	886C>T	F
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	941	891T>G	S
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	941	891T>G	S
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	1076	1026A>T	S
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	1373	1323G>A	F
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	1460	1410C>T	S
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	1460	1410C>T	S
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	1609	1559A>G	K520R
M71246	M71246	None	GEN-3KO	Interferon alpha 17	131	131A>C	H44P
M71246	M71246	None	GEN-3KO	Interferon alpha 17	483	483C>T	S
M71246	M71246	None	GEN-3KO	Interferon alpha 17	512	512G>T	R171I
M73700	M73700	150210	GEN-S6	Human neutrophil lactoferrin mRNA, complete cds and 5' promoter region	2673	85G>A	A29T
M73700	M73700	150210	GEN-S6	Human neutrophil lactoferrin mRNA, complete cds and 5' promoter region	3090	502G>A	V168M
M73700	M73700	150210	GEN-S6	Human neutrophil lactoferrin mRNA, complete cds and 5' promoter region	4101	1513G>A	D505N
M73700	M73700	150210	GEN-S6	Human neutrophil lactoferrin mRNA, complete cds and 5' promoter region	4211	1623T>C	S
M73700	M73700	150210	GEN-S6	Human neutrophil lactoferrin mRNA, complete cds and 5' promoter region	4325	1737G>C	E579D
M73700	M73700	150210	GEN-S6	Human neutrophil lactoferrin mRNA, complete cds and 5' promoter region	4482	1894C>T	S
M74782	M74782	308385	GEN-64	Interleukin 3 receptor, alpha	1396	1250C>T	3

CD79B	M80461	147245	GEN-3UT	(low affinity) Human B29 mRNA, complete cds	795	781C>T	3
CD79B	M80461	147245	GEN-3UT	Human B29 mRNA, complete cds	804	790C>A	3
CD79B	M80461	147245	GEN-3UT	Human B29 mRNA, complete cds	1033	1019C>T	3
M80462	M80462	112205	GEN-3US	Human MB-1 mRNA, complete cds	241	205G>A	V69I
M80646	M80646	274180	GEN-40	Thromboxane synthase	756	585G>C	S
M80646	M80646	274180	GEN-40	Thromboxane synthase	1240	1069C>G	L357V
CD34	M81104	142230	GEN-3VN	Human CD34 mRNA, complete cds	1338	1045A>G	K349E
CD34	M81104	142230	GEN-3VN	Human CD34 mRNA, complete cds	2490	2197G>A	3
M81590	M81590	182131	GEN-3VZ	Serotonin 5-HT receptors 5-HT1D	190	129C>T	S
M81590	M81590	182131	GEN-3VZ	Serotonin 5-HT receptors 5-HT1D	432	371T>G	F124C
M81590	M81590	182131	GEN-3VZ	Serotonin 5-HT receptors 5-HT1D	922	861G>C	S
M81590	M81590	182131	GEN-3VZ	Serotonin 5-HT receptors 5-HT1D	1241	1180G>A	3
M81695	M81695	151510	GEN-17	Leukocyte integrin alpha-x	1834	1770G>C	S
M81695	M81695	151510	GEN-17	Leukocyte integrin alpha-x	3282	3218C>T	T1073M
M81695	M81695	151510	GEN-17	Leukocyte integrin alpha-x	4213	4149C>G	3
TAC1R	M81797	162323	GEN-3W8	Tachylinins NK1 receptor	696	652G>A	V218I
TAC1R	M81797	162323	GEN-3W8	Tachylinins NK1 receptor	1397	1353G>C	3
M83566	M83566	114206	GEN-3Y7	Human neuroendocrine/beta-cell- type calcium channel alpha-1 subunit mRNA, complete cds	1222	1104C>T	S
M83566	M83566	114206	GEN-3Y7	Human neuroendocrine/beta-cell- type calcium channel alpha-1 subunit mRNA, complete cds	1468	1350G>A	S

CHRNA5	M83712	118505	GEN-3YQ	Nicotinic, Cholinergic receptor alpha 5	1340	1192G>A	D398N
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA-A 0201) mRNA, complete cds	28	28G>C	V10L
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA-A 0201) mRNA, complete cds	98	98T>A	F33Y
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA-A 0201) mRNA, complete cds	102	102A>C	S
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA-A 0201) mRNA, complete cds	144	144A>C	S
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA-A 0201) mRNA, complete cds	240	240T>G	S
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA-A 0201) mRNA, complete cds	257	257G>A	G86E
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA-A 0201) mRNA, complete cds	292	292C>G	H98D
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA-A 0201) mRNA, complete cds	362	362G>T	R121M
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA-A 0201) mRNA, complete cds	391	391T>G	W131G
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA-A 0201) mRNA, complete cds	418	418T>G	Y140D

M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA-A 0201) mRNA, complete cds	453	453A>C	K151N
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA-A 0201) mRNA, complete cds	527	527T>A	V176E
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA-A 0201) mRNA, complete cds	539	539T>G	L180W
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA-A 0201) mRNA, complete cds	622	622G>C	A208P
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA-A 0201) mRNA, complete cds	630	630A>G	S
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA-A 0201) mRNA, complete cds	666	666A>G	S
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA-A 0201) mRNA, complete cds	762	762C>T	S
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA-A 0201) mRNA, complete cds	789	789A>G	S
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA-A 0201) mRNA, complete cds	806	806C>T	A269V
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA-A 0201) mRNA, complete cds	807	807G>A	S

M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA- A 0201) mRNA, complete cgs	808	808G>T	A270S
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA- A 0201) mRNA, complete cgs	819	819G>A	S
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA- A 0201) mRNA, complete cgs	829	829C>G	Q277E
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA- A 0201) mRNA, complete cgs	868	868T>C	S
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA- A 0201) mRNA, complete cgs	870	870G>C	L290F
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA- A 0201) mRNA, complete cgs	900	900G>A	S
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA- A 0201) mRNA, complete cgs	901	901T>G	S301A
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA- A 0201) mRNA, complete cgs	916	916A>G	I306V
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA- A 0201) mRNA, complete cgs	945	945G>A	S
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA- A 0201) mRNA, complete cgs	952	952T>C	F318L
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA- A 0201) mRNA, complete cgs	967	967A>G	T323A

M84379	M84379	142800	GEN-SA	lymphocyte antigen (HLA-A 0201) mRNA, complete cds	987	987T>C	S
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA-A 0201) mRNA, complete cds	992	992T>G	M331R
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA-A 0201) mRNA, complete cds	1005	1005G>C	K335N
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA-A 0201) mRNA, complete cds	1013	1013A>G	D338G
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA-A 0201) mRNA, complete cds	1029	1029C>T	S
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA-A 0201) mRNA, complete cds	1033	1033T>A	S345T
M84379	M84379	142800	GEN-SA	Human MHC class I lymphocyte antigen (HLA-A 0201) mRNA, complete cds	1072	1072G>A	V358M
M84526	M84526	134350	GEN-3ZL	Human adipsin/complement factor D mRNA, complete cds	46	(-9)C>T	5
M84526	M84526	134350	GEN-3ZL	Human adipsin/complement factor D mRNA, complete cds	399	345C>A	S
M84526	M84526	134350	GEN-3ZL	Human adipsin/complement factor D mRNA, complete cds	408	354A>G	S
M84526	M84526	134350	GEN-3ZL	Human adipsin/complement factor D mRNA, complete cds	859	805C>T	3

M84526	M84526	134350	3ZL	adipsin/complement factor D mRNA, complete cds	Human	891	837G>C	3
M84747	M84747	300007	GEN-3ZL	adipsin/complement factor D mRNA, complete cds		1273	1094G>A	R365H
TGFBR2	M85079	190182	GEN-3ZS	Human TGF-beta type II receptor mRNA, complete cds		2045	1710A>C	3
YWHAZ	M86400	601288	GEN-40Y	Human phospholipase A2 mRNA, complete cds		1653	1569T>A	3
YWHAZ	M86400	601288	GEN-40Y	Human phospholipase A2 mRNA, complete cds		2599	2515C>G	3
YWHAZ	M86400	601288	GEN-40Y	Human phospholipase A2 mRNA, complete cds		2619	2535A>C	3
YWHAZ	M86400	601288	GEN-40Y	Human phospholipase A2 mRNA, complete cds		2656	2572A>C	3
YWHAZ	M86400	601288	GEN-40Y	Human phospholipase A2 mRNA, complete cds		2745	2661C>T	3
YWHAZ	M86400	601288	GEN-40Y	Human phospholipase A2 mRNA, complete cds		2761	2677A>C	3
M86511	M86511	158120	GEN-419	Human monocyte antigen CD14 (CD14) mRNA, complete cds		1142	1067C>A	T356N
M86511	M86511	158120	GEN-419	Human monocyte antigen CD14 (CD14) mRNA, complete cds		1176	1101G>C	S
M87503	M87503	None	GEN-443	Human IFN-responsive transcription factor subunit mRNA, complete cds		1424	1390T>A	3
M87503	M87503	None	GEN-443	Human IFN-responsive transcription factor subunit mRNA, complete cds		1524	1490A>C	3
M89473	M89473	None	GEN-4FU	NEUROMEDIN K RECEPTOR		1614	1471T>C	3
M90100	M90100	600262	GEN-1A	Cyclooxygenase 2 COX2		2159	2062G>C	3
M90100	M90100	600262	GEN-1A	Cyclooxygenase 2 COX2		2186	2089-2094ATATTA	3
M90100	M90100	600262	GEN-1A	Cyclooxygenase 2 COX2		2186	>ATATTA	3
							2094delATAT	

M90100	M90100	600262	GEN-1A	Cyclooxygenase 2 COX2	2230	2133A>G	3
M90100	M90100	600262	GEN-1A	Cyclooxygenase 2 COX2	2339	2242T>C	3
M90100	M90100	600262	GEN-1A	Cyclooxygenase 2 COX2	2409	2312G>A	3
M90100	M90100	600262	GEN-1A	Cyclooxygenase 2 COX2	2726	2629C>T	3
M90100	M90100	600262	GEN-1A	Cyclooxygenase 2 COX2	2983	2886C>T	3
M92269	M92269	114205	GEN-SV	Ca Channel alpha1c (alt. splice) L-Type	3846	3846C>T	S
M92269	M92269	114205	GEN-SV	Ca Channel alpha1c (alt. splice) L-Type	5505	5505G>A	S
M92269	M92269	114205	GEN-SV	Ca Channel alpha1c (alt. splice) L-Type	6582	6582A>G	S
M92269	M92269	114205	GEN-SV	Ca Channel alpha1c (alt. splice) L-Type	6613	6613G>C	G2205R
M92269	M92269	114205	GEN-SV	Ca Channel alpha1c (alt. splice) L-Type	6614	6614G>C	G2205A
M92303	M92303	114207	GEN-1C	L-Type voltage sensitive channel beta-1	860	711G>A	S
IL8RB	M94582	146928	GEN-49G	Interleukin 8 receptor	838	786T>C	S
IL8RB	M94582	146928	GEN-49G	Interleukin 8 receptor	1262	1210C>T	3
IL8RB	M94582	146928	GEN-49G	Interleukin 8 receptor	1494	1442A>G	3
M95678	M95678	604114	GEN-4A6	Homo sapiens phospholipase C-beta-2 mRNA, complete cds	1346	1182T>C	S
M95678	M95678	604114	GEN-4A6	Homo sapiens phospholipase C-beta-2 mRNA, complete cds	3436	3272A>G	E1091G
M95678	M95678	604114	GEN-4A6	Homo sapiens phospholipase C-beta-2 mRNA, complete cds	4137	3973C>T	3
M95708	M95708	107271	GEN-SF	Homo sapiens Ly-6-like protein (CD59) mRNA, complete cds	497	435C>T	3
M96652	M96652	147851	GEN-65	Interleukin 5 receptor alpha	883	634T>G	S212A
M96954	M96954	603413	GEN-4B5	Homo sapiens nucleolysin TIAR mRNA, complete cds	957	912A>C	Q304H
ID2	M97796	600386	GEN-	Human helix-loop-helix	402	294C>G	S

M98045	M98045	136510	4C0	protein (ld-2) mRNA, complete cds	802	732C>T	S
M98045	M98045	136510	GEN-4C3	Homo sapiens folypolyglutamate synthetase mRNA, complete cds	1747	1677G>T	3
M98045	M98045	136510	GEN-4C3	Homo sapiens folypolyglutamate synthetase mRNA, complete cds	1900	1830T>C	3
M98045	M98045	136510	GEN-4C3	Homo sapiens folypolyglutamate synthetase mRNA, complete cds	1900	1830T>C	3
M98045	M98045	136510	GEN-4C3	Homo sapiens folypolyglutamate synthetase mRNA, complete cds	1912	1842G>A	3
M98045	M98045	136510	GEN-4C3	Homo sapiens folypolyglutamate synthetase mRNA, complete cds	1995	1925C>G	3
S46622	S46622	114107	GEN-1F	Calcineurin A-gamma	1893	1607C>G	3
S46622	S46622	114107	GEN-1F	Calcineurin A-gamma	1941	1655A>G	3
S57235	S57235	153634	GEN-37N	CD68=110kda transmembrane glycoprotein [human, promonocyte cell line U937, mRNA, 1722 nt]	775	760A>C	K254Q
U00672	U00672	146933	GEN-4A	Interleukin 10 receptor	3377	3316A>C	3
U00672	U00672	146933	GEN-4A	Interleukin 10 receptor	3524	3463A>G	3
U02882	U02882	600129	GEN-XU	Human rolipram-sensitive 3,5-cyclic AMP phosphodiesterase mRNA, complete cds	1798	1690T>C	C564R
U02882	U02882	600129	GEN-XU	Human rolipram-sensitive 3,5-cyclic AMP	1881	1773G>A	S

U02882	U02882	600129	GEN-XU	phosphodiesterase mRNA, complete cds	4691	4583T>G	3
U03858	U03858	600007	GEN-MDM	Human rolipram-sensitive 3,5-cyclic AMP phosphodiesterase mRNA, complete cds	683	600C>T	S
U03858	U03858	600007	GEN-MDM	Fms-related tyrosine kinase 3 ligand	1016	933T>C	3
U03882	U03882	601267	GEN-12B	Fms-related tyrosine kinase 3 ligand Human monocyte chemoattractant protein 1 receptor (MCP-1RA) alternatively spliced mRNA, complete cds	1436	1397G>A	3
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	38	15C>T	S
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	282	259A>T	S87C
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	350	327C>T	S
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	365	342T>C	S
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	464	441G>A	S
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	474	451A>G	M151V
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	532	509A>G	H170R
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	538	515T>A	L172Q
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	689	666T>C	S

DDH1	U05598	600450	GEN-184	complete cds Human dihydrodiol dehydrogenase mRNA,	806	783G>A	S
DDH1	U05598	600450	GEN-184	complete cds Human dihydrodiol dehydrogenase mRNA,	872	849G>T	S
DDH1	U05598	600450	GEN-184	complete cds Human dihydrodiol dehydrogenase mRNA,	952	929T>G	I310S
DDH1	U05598	600450	GEN-184	complete cds Human dihydrodiol dehydrogenase mRNA,	1020	997G>A	3
DDH1	U05598	600450	GEN-184	complete cds Human dihydrodiol dehydrogenase mRNA,	1035	1012G>A	3
DDH1	U05598	600450	GEN-184	complete cds Human dihydrodiol dehydrogenase mRNA,	1112	1089C>T	3
U05875	U05875	147569	GEN-18J	complete cds Human clone pSK1 interferon gamma receptor accessory factor-1 (AF-1)	2047	1399C>G	3
U05875	U05875	147569	GEN-18J	complete cds Human clone pSK1 interferon gamma receptor accessory factor-1 (AF-1)	2087	1439T>C	3
XDH	U06117	278300	GEN-194	mRNA, complete cds Human xanthine dehydrogenase (XDH)	3951	3888C>G	S
U07225	U07225	600041	GEN-1DM	mRNA, complete cds P2Y2 purinoceptor	2008	1763G>A	3
U07989	U07989	None	GEN-Q2	Human Burkitts lymphoma immunoglobulin kappa light chain mRNA, partial cds	39	39T>A	S
U07989	U07989	None	GEN-Q2	Human Burkitts lymphoma immunoglobulin kappa light chain mRNA, partial cds	307	307G>C	V103L
U07989	U07989	None	GEN-Q2	Human Burkitts lymphoma immunoglobulin kappa light chain mRNA, partial cds	312	312A>G	S

U07989	U07989	None	GEN-Q2	Human Burkitts lymphoma immunoglobulin kappa light chain mRNA, partial cds	568	568G>C	V190L
U07989	U07989	None	GEN-Q2	Human Burkitts lymphoma immunoglobulin kappa light chain mRNA, partial cds	610	610G>A	V204I
U08015	U08015	600489	GEN-1FD	Human NF-ATc mRNA, complete cds	530	291C>T	S
U08015	U08015	600489	GEN-1FD	Human NF-ATc mRNA, complete cds	1094	855G>A	S
U08015	U08015	600489	GEN-1FD	Human NF-ATc mRNA, complete cds	2222	1983G>A	S
U08015	U08015	600489	GEN-1FD	Human NF-ATc mRNA, complete cds	2225	1986A>G	S
U08015	U08015	600489	GEN-1FD	Human NF-ATc mRNA, complete cds	2295	2056A>C	S686R
U09117	U09117	602142	GEN-1GC	Phospholipase C delta-1	333	239G>A	R80H
U09117	U09117	602142	GEN-1GC	Phospholipase C delta-1	460	366G>A	S
U09117	U09117	602142	GEN-1GC	Phospholipase C delta-1	1858	1764G>A	S
SLC18A3	U09210	600336	GEN-4F3	Human vesicular acetylcholine transporter mRNA, complete cds	838	396T>C	S
SLC18A3	U09210	600336	GEN-4F3	Human vesicular acetylcholine transporter mRNA, complete cds	1369	927A>G	S
SLC18A3	U09210	600336	GEN-4F3	Human vesicular acetylcholine transporter mRNA, complete cds	1567	1125C>G	S
SLC18A3	U09210	600336	GEN-4F3	Human vesicular acetylcholine transporter mRNA, complete cds	2080	1638G>T	3
SLC18A3	U09210	600336	GEN-4F3	Human vesicular acetylcholine transporter mRNA, complete cds	2199	1757G>A	3
SLC18A3	U09210	600336	GEN-4F3	Human vesicular acetylcholine transporter mRNA, complete cds	2349	1907G>T	3
U09607	U09607	600173	GEN-	Janus kinase 3 (a protein	1925	1830G>A	M610I

U09759	U09759	602896	MKU GEN- 1HA	tyrosine kinase, leukocyte) Human protein kinase (JNK2) mRNA, complete cds	303	152A>G	N51S
U09759	U09759	602896	GEN- 1HA	Human protein kinase (JNK2) mRNA, complete cds	1079	928A>G	I310V
U09759	U09759	602896	GEN- 1HA	Human protein kinase (JNK2) mRNA, complete cds	1280	1129C>T	P377S
U09759	U09759	602896	GEN- 1HA	Human protein kinase (JNK2) mRNA, complete cds	1559	1408C>T	3
U09806	U09806	None	GEN- 4FZ	Human methylenetetrahydrofolate reductase mRNA, partial cds	120	120T>C	S
U09806	U09806	None	GEN- 4FZ	Human methylenetetrahydrofolate reductase mRNA, partial cds	473	473G>A	R158Q
U09806	U09806	None	GEN- 4FZ	Human methylenetetrahydrofolate reductase mRNA, partial cds	550	550C>T	F
U09806	U09806	None	GEN- 4FZ	Human methylenetetrahydrofolate reductase mRNA, partial cds	668	668C>T	A223V
U09806	U09806	None	GEN- 4FZ	Human methylenetetrahydrofolate reductase mRNA, partial cds	1059	1059T>C	S
U09806	U09806	None	GEN- 4FZ	Human methylenetetrahydrofolate reductase mRNA, partial cds	1289	1289C>A	E430A
U09806	U09806	None	GEN- 4FZ	Human methylenetetrahydrofolate reductase mRNA, partial cds	1308	1308T>C	3

OPRD1	U10504	165195	GEN-4F5	Human delta opiate receptor mRNA, complete cds	921	921T>C	S
U11276	U11276	602890	GEN-1K3	Human hNKR-P1a protein (NKR-P1A) mRNA, complete cds	563	503T>C	I168T
TPMT	U12387	187680	GEN-1LY	Human thiopurine methyltransferase (TPMT) mRNA, complete cds	536	460G>A	A154T
TPMT	U12387	187680	GEN-1LY	Human thiopurine methyltransferase (TPMT) mRNA, complete cds	795	719A>G	Y240C
TPMT	U12387	187680	GEN-1LY	Human thiopurine methyltransferase (TPMT) mRNA, complete cds	1085	1009T>C	3
TPMT	U12387	187680	GEN-1LY	Human thiopurine methyltransferase (TPMT) mRNA, complete cds	1336	1260C>T	3
TPMT	U12387	187680	GEN-1LY	Human thiopurine methyltransferase (TPMT) mRNA, complete cds	1373	1297G>A	3
U12507	U12507	600681	GEN-1MD	Cardiac inward rectifier potassium channel (HH-IRK1)	338	13C>A	S
U12507	U12507	600681	GEN-1MD	Cardiac inward rectifier potassium channel (HH-IRK1)	1597	1272G>A	S
U12597	U12597	601895	GEN-4E	tumor necrosis factor type 2 receptor associated protein (TRAP3)	2182	2128G>T	3
U13737	U13737	600636	GEN-1PC	Human cysteine protease CPP32 isoform alpha mRNA, complete cds	2356	2132A>C	3
U13737	U13737	600636	GEN-1PC	Human cysteine protease CPP32 isoform alpha mRNA, complete cds	2535	2311C>T	3
U14510	U14510	602698	GEN-1RD	Human transcription factor NFATx mRNA, complete cds	2128	2104A>C	M702L
U14510	U14510	602698	GEN-1RD	Human transcription factor NFATx mRNA, complete cds	2516	2492T>G	L831W

U14510	U14510	602698	GEN- 1RD	Human transcription factor NFATx mRNA, complete cds	2720	2696C>G	A899G
U14510	U14510	602698	GEN- 1RD	Human transcription factor NFATx mRNA, complete cds	2792	2768C>T	A923V
U14510	U14510	602698	GEN- 1RD	Human transcription factor NFATx mRNA, complete cds	2828	2804C>G	A935G
U14510	U14510	602698	GEN- 1RD	Human transcription factor NFATx mRNA, complete cds	2903	2879C>G	A960G
U14510	U14510	602698	GEN- 1RD	Human transcription factor NFATx mRNA, complete cds	2967	2943G>A	S
U14510	U14510	602698	GEN- 1RD	Human transcription factor NFATx mRNA, complete cds	3333	3309G>A	3
U14510	U14510	602698	GEN- 1RD	Human transcription factor NFATx mRNA, complete cds	3577	3553G>A	3
U14650	U14650	602243	GEN- 1RL	Human platelet-endothelial tetraspan antigen 3 mRNA, complete cds	638	579A>G	S
U14650	U14650	602243	GEN- 1RL	Human platelet-endothelial tetraspan antigen 3 mRNA, complete cds	1048	989G>A	3
U14650	U14650	602243	GEN- 1RL	Human platelet-endothelial tetraspan antigen 3 mRNA, complete cds	1171	1112T>C	3
U14650	U14650	602243	GEN- 1RL	Human platelet-endothelial tetraspan antigen 3 mRNA, complete cds	1263	1204G>C	3
U14650	U14650	602243	GEN- 1RL	Human platelet-endothelial tetraspan antigen 3 mRNA, complete cds	1301	1242C>T	3
U14650	U14650	602243	GEN- 1RL	Human platelet-endothelial tetraspan antigen 3 mRNA, complete cds	1351	1292T>C	3
U14650	U14650	602243	GEN- 1RL	Human platelet-endothelial tetraspan antigen 3 mRNA, complete cds	1389	1330A>T	3

U14650	U14650	602243	GEN-1RL	tetraspan antigen 3 mRNA, complete cds	1404	1345G>A	3
U15637	U15637	601896	GEN-1U8	Human platelet-endothelial tetraspan antigen 3 mRNA, complete cds	596	386T>C	M129T
U15637	U15637	601896	GEN-1U8	Human CD40 binding protein (CD40bp) mRNA, complete cds	1317	1107C>T	S
U16031	U16031	None	GEN-HX	Human CD40 binding protein (CD40bp) mRNA, complete cds	2964	2799G>A	3
SDF1	U16752	600835	GEN-1YK	Transcription Factor IL-4 Stat	47	(-34)C>T	5
SDF1	U16752	600835	GEN-1YK	Human cytokine SDF-1-beta mRNA, complete cds	2927	2847G>C	3
SDF1	U16752	600835	GEN-1YK	Human cytokine SDF-1-beta mRNA, complete cds	3159	3079T>C	3
SDF1	U16752	600835	GEN-1YK	Human cytokine SDF-1-beta mRNA, complete cds	3294	3214T>G	3
NOS1	U17327	163731	GEN-209	Human cytokine SDF-1-beta mRNA, complete cds	3391	2706C>T	S
PDE4A	U18087	600126	GEN-214	Human neuronal nitric oxide synthase (NOS1) mRNA, complete cds	642	633T>G	S
PDE4A	U18087	600126	GEN-214	Human 3,5-cyclic AMP phosphodiesterase HPDE4A6 mRNA, complete cds	804	795T>C	S
PDE4A	U18087	600126	GEN-214	Human 3,5-cyclic AMP phosphodiesterase HPDE4A6 mRNA, complete cds	1616	1607A>C	E536A
U18242	U18242	601118	GEN-1N	Human 3,5-cyclic AMP phosphodiesterase HPDE4A6 mRNA, complete cds	1117	1081T>G	3
U19487	U19487	176804	GEN-4I	Cyclophilin Ligand (calcium modulating) PROTAGLANDIN E2 RECEPTOR, EP2 SUBTYPE	85	(-72)A>G	5

U19487	U19487	176804	GEN-4I	PROSTAGLANDIN E2 RECEPTOR, EP2 SUBTYPE	231	75A>T	S
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	53	(-43)T>C	5
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	175	80G>A	R27H
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	175	80G>A	R27H
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	341	246C>G	S
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	791	696C>T	S
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	1067	972G>A	S
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	2100	2005*2006ins G	F
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	2582	248TT>G	3
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	2582	2487T>G	3
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	2617	2522C>T	3
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	2617	2522C>T	3
U19720	U19720	600424	GEN-I1	Folate Transporter (SLC19A1)	2652	2557T>C	3
U19775	U19775	600289	GEN- 22C	Human MAP kinase Mxi2 (MXI2) mRNA, complete cds	731	688G>A	D230N
U20157	U20157	601690	GEN-234	Human platelet-activating factor acetylhydrolase mRNA, complete cds	1297	1136T>C	V379A
U20350	U20350	602237	GEN-239	Human G protein-coupled receptor V28 mRNA, complete cds	1304	1217T>C	3
U20536	U20536	601532	GEN- 23K	Human cysteine protease Mch2 isoform alpha (Mch2) mRNA, complete cds	982	904C>T	3
U20536	U20536	601532	GEN- 23K	Human cysteine protease Mch2 isoform alpha (Mch2) mRNA, complete cds	1117	1039G>A	3

U20536	U20536	601532	GEN-23K	mRNA, complete cds Human cysteine protease Mch2 isoform alpha (Mch2)	1322	1244T>C	3
U20536	U20536	601532	GEN-23K	mRNA, complete cds Human cysteine protease Mch2 isoform alpha (Mch2)	1363	1285T>C	3
U21847	U21847	601878	GEN-252	mRNA, complete cds Human TGF-beta inducible early protein (TIEG)	986	900C>T	S
U21847	U21847	601878	GEN-252	mRNA, complete cds Human TGF-beta inducible early protein (TIEG)	1670	1584C>T	3
U21847	U21847	601878	GEN-252	mRNA, complete cds Human TGF-beta inducible early protein (TIEG)	2542	2456A>C	3
U23143	U23143	138450	GEN-M1Y	mRNA, complete cds Human mitochondrial serine hydroxymethyltransferase gene, nuclear encoded mitochondrion protein, complete cds	506	506T>G	F169C
U25029	U25029	138040	GEN-82	Glucocorticoid receptor alpha	335	335C>T	3
U25029	U25029	138040	GEN-82	Glucocorticoid receptor alpha	386	386T>C	3
U25029	U25029	138040	GEN-82	Glucocorticoid receptor alpha	1069	1069C>T	3
U27467	U27467	601056	GEN-2BX	Human Bcl-2 related (Bfl-1) mRNA, complete cds	476	442T>C	F148L
U27467	U27467	601056	GEN-2BX	Human Bcl-2 related (Bfl-1) mRNA, complete cds	481	447A>G	S
U27467	U27467	601056	GEN-2BX	Human Bcl-2 related (Bfl-1) mRNA, complete cds	542	508C>G	L170V
U27467	U27467	601056	GEN-2BX	Human Bcl-2 related (Bfl-1) mRNA, complete cds	578	544C>T	3
U27467	U27467	601056	GEN-2BX	Human Bcl-2 related (Bfl-1) mRNA, complete cds	614	580T>C	3
U27467	U27467	601056	GEN-2BX	Human Bcl-2 related (Bfl-1) mRNA, complete cds	616	582G>A	3
CSNK1D	U29171	600864	GEN-	mRNA, complete cds Human casein kinase I	1612	1435C>A	3

U31628	U31628	601070	2E2 GEN-4J	delta mRNA, complete cds	1250	1168G>T	3
U32324	U32324	600939	GEN-4K	Interleukin 15 receptor alpha chain	1266	1205C>A	P402Q
U32324	U32324	600939	GEN-4K	interleukin 11 receptor alpha chain	1513	1452C>T	3
U32989	U32989	191070	GEN- 2JH	interleukin 11 receptor alpha chain	991	927G>A	S
U33017	U33017	603492	GEN- 2JO	Human tryptophan oxygenase (TDO) mRNA, complete cds	1489	1356A>T	3
U33017	U33017	603492	GEN- 2JO	Human signaling lymphocytic activation molecule (SLAM) mRNA, complete cds	1661	1528C>T	3
U37448	U37448	601761	GEN- 2OC	Human signaling lymphocytic activation molecule (SLAM) mRNA, complete cds	736	693G>A	S
U37448	U37448	601761	GEN- 2OC	Human Mch3 isoform alpha (Mch3) mRNA, complete cds	1285	1242T>C	3
U37448	U37448	601761	GEN- 2OC	Human Mch3 isoform alpha (Mch3) mRNA, complete cds	1294	1251T>C	3
U37448	U37448	601761	GEN- 2OC	Human Mch3 isoform alpha (Mch3) mRNA, complete cds	1580	1537A>T	3
U37448	U37448	601761	GEN- 2OC	Human Mch3 isoform alpha (Mch3) mRNA, complete cds	1621	1578G>T	3
U37448	U37448	601761	GEN- 2OC	Human Mch3 isoform alpha (Mch3) mRNA, complete cds	1715	1672G>A	3
U37448	U37448	601761	GEN- 2OC	Human Mch3 isoform alpha (Mch3) mRNA, complete cds	1764	1721G>A	3
U37518	U37518	None	GEN- 2OG	Human Mch3 isoform alpha (Mch3) mRNA, complete cds	912	825C>T	S
				Human TNF-related apoptosis inducing ligand			

U37518	U37518	None	GEN-2OG	TRAIL mRNA, complete cds	1140	1053A>G	3
U37518	U37518	None	GEN-2OG	Human TNF-related apoptosis inducing ligand TRAIL mRNA, complete cds	1289	1202C>A	3
U37518	U37518	None	GEN-2OG	Human TNF-related apoptosis inducing ligand TRAIL mRNA, complete cds	1525	1438G>A	3
U37518	U37518	None	GEN-2OG	Human TNF-related apoptosis inducing ligand TRAIL mRNA, complete cds	1588	1501G>A	3
U37518	U37518	None	GEN-2OG	Human TNF-related apoptosis inducing ligand TRAIL mRNA, complete cds	1595	1508C>T	3
TAC2	U37529	162320	GEN-2OH	Substance P beta-PPT-A	644	499G>A	3
TAC2	U37529	162320	GEN-2OH	Substance P beta-PPT-A	694	549T>C	3
TAC2	U37529	162320	GEN-2OH	Substance P beta-PPT-A	799	654A>G	3
TAC2	U37529	162320	GEN-2OH	Substance P beta-PPT-A	826	681C>T	3
U39656	U39656	601254	GEN-2Q8	Human MAP kinase kinase 6 (MKK6) mRNA, complete cds	431	91A>C	S
U39656	U39656	601254	GEN-2Q8	Human MAP kinase kinase 6 (MKK6) mRNA, complete cds	713	373G>A	V125M
U40038	U40038	600998	GEN-7O	Guanine nucleotide binding protein (G protein), q polypeptide	825	783C>T	S
U40038	U40038	600998	GEN-7O	Guanine nucleotide binding protein (G protein), q	878	836T>C	L279P

U40038	U40038	600998	GEN-7O	Guanine nucleotide binding protein (G protein), q polypeptide	1029	987G>A	S
U40038	U40038	600998	GEN-7O	Guanine nucleotide binding protein (G protein), q polypeptide	1051	1009A>G	I337V
U40038	U40038	600998	GEN-7O	Guanine nucleotide binding protein (G protein), q polypeptide	1068	1026T>A	S
U40038	U40038	600998	GEN-7O	Guanine nucleotide binding protein (G protein), q polypeptide	1093	1051T>C	S
U40282	U40282	602366	GEN-2RJ	Homo sapiens integrin-linked kinase (ILK) mRNA, complete cds	453	297C>T	S
U40282	U40282	602366	GEN-2RJ	Homo sapiens integrin-linked kinase (ILK) mRNA, complete cds	975	819G>A	S
U40282	U40282	602366	GEN-2RJ	Homo sapiens integrin-linked kinase (ILK) mRNA, complete cds	1580	1424G>A	3
U40282	U40282	602366	GEN-2RJ	Homo sapiens integrin-linked kinase (ILK) mRNA, complete cds	1670	1514G>C	3
U40282	U40282	602366	GEN-2RJ	Homo sapiens integrin-linked kinase (ILK) mRNA, complete cds	1769	1613A>C	3
U40347	U40347	600950	GEN-2RK	Human serotonin N-acetyltransferase mRNA, complete cds	382	148G>A	E50K
U40583	U40583	118511	GEN-4O	Nicotinic, Cholinergic receptor alpha 7	661	654T>C	S
U40583	U40583	118511	GEN-4O	Nicotinic, Cholinergic receptor alpha 7	697	690A>G	S
U40583	U40583	118511	GEN-4O	Nicotinic, Cholinergic receptor alpha 7	940	933G>A	S
U40583	U40583	118511	GEN-4O	Nicotinic, Cholinergic receptor alpha 7	1276	1269T>C	S
U40583	U40583	118511	GEN-4O	Nicotinic, Cholinergic receptor alpha 7	1790	1783A>T	3

U40583	U40583	118511	GEN-4O	Nicotinic, Cholinergic receptor alpha 7	1792	1785T>A	3
U43030	U43030	600435	GEN-LFI	Human cardiotrophin-1 (CTF1) mRNA, complete cds	1404	1372C>T	3
U43142	U43142	601528	GEN- 2UM	Human vascular endothelial growth factor related protein VRP mRNA, complete cds	1499	1128C>T	S
LEPR	U43168	601007	GEN- 2UN	Human leptin receptor (Ob- r) mRNA, complete cds	446	253A>G	T85A
LEPR	U43168	601007	GEN- 2UN	Human leptin receptor (Ob- r) mRNA, complete cds	519	326A>G	K109R
LEPR	U43168	601007	GEN- 2UN	Human leptin receptor (Ob- r) mRNA, complete cds	861	668A>G	Q223R
LEPR	U43168	601007	GEN- 2UN	Human leptin receptor (Ob- r) mRNA, complete cds	1222	1029T>C	S
LEPR	U43168	601007	GEN- 2UN	Human leptin receptor (Ob- r) mRNA, complete cds	2161	1968G>C	K656N
LEPR	U43168	601007	GEN- 2UN	Human leptin receptor (Ob- r) mRNA, complete cds	2174	1981A>C	T661P
LEPR	U43168	601007	GEN- 2UN	Human leptin receptor (Ob- r) mRNA, complete cds	2764	2571T>G	S
LEPR	U43168	601007	GEN- 2UN	Human leptin receptor (Ob- r) mRNA, complete cds	3151	2958C>T	S
LEPR	U43168	601007	GEN- 2UN	Human leptin receptor (Ob- r) mRNA, complete cds	3250	3057G>A	S
U45448	U45448	600845	GEN-4FI	Human P2x1 receptor mRNA, complete cds	1424	1228A>G	3
U45448	U45448	600845	GEN-4FI	Human P2x1 receptor mRNA, complete cds	1604	1408C>G	3
U45448	U45448	600845	GEN-4FI	Human P2x1 receptor mRNA, complete cds	1719	1523G>A	3
U45448	U45448	600845	GEN-4FI	Human P2x1 receptor mRNA, complete cds	1827	1631G>A	3
U45448	U45448	600845	GEN-4FI	Human P2x1 receptor mRNA, complete cds	2286	2090G>A	3
SCYA11	U46573	601156	GEN- 2WZ	Human eotaxin precursor mRNA, complete cds	120	67G>A	A23T
SCYA11	U46573	601156	GEN- 2WZ	Human eotaxin precursor mRNA, complete cds	554	501T>C	3

SD-144146.1

U47634	U47634	None	GEN-2XR	Human beta-tubulin class III isotype (beta-3) mRNA, complete cds	1005	1005C>T	S
U47634	U47634	None	GEN-2XR	Human beta-tubulin class III isotype (beta-3) mRNA, complete cds	1035	1035C>T	S
U47634	U47634	None	GEN-2XR	Human beta-tubulin class III isotype (beta-3) mRNA, complete cds	1431	1431T>C	3
U47634	U47634	None	GEN-2XR	Human beta-tubulin class III isotype (beta-3) mRNA, complete cds	1502	1502G>A	3
U49516	U49516	312861	GEN-1Q	Serotonin 5-HT receptors 5-HT2C	2915	2187A>C	3
U49516	U49516	312861	GEN-1Q	Serotonin 5-HT receptors 5-HT2C	2947	2219A>G	3
U50040	U50040	601582	GEN-2ZR	Human signaling inositol polyphosphate 5 phosphatase SIP-110 mRNA, complete cds	196	180A>G	S
U50040	U50040	601582	GEN-2ZR	Human signaling inositol polyphosphate 5 phosphatase SIP-110 mRNA, complete cds	418	402C>G	S
U50040	U50040	601582	GEN-2ZR	Human signaling inositol polyphosphate 5 phosphatase SIP-110 mRNA, complete cds	2613	2597C>A	P866H
U50040	U50040	601582	GEN-2ZR	Human signaling inositol polyphosphate 5 phosphatase SIP-110 mRNA, complete cds	2638	2622G>A	S
U50040	U50040	601582	GEN-2ZR	Human signaling inositol polyphosphate 5 phosphatase SIP-110 mRNA, complete cds	2882	2866C>T	H956Y
U50040	U50040	601582	GEN-2ZR	Human signaling inositol polyphosphate 5 phosphatase SIP-110 mRNA, complete cds	3193	3177C>T	3
U50040	U50040	601582	GEN-2ZR	Human signaling inositol polyphosphate 5 phosphatase SIP-110 mRNA, complete cds	3222	3206C>T	3

U50040	IRF4	U50040	601582	2ZR	polyphosphate 5 phosphatase SIP-110 mRNA, complete cds	3863	3847G>A	3
		GEN- 2ZR			Human signaling inositol polyphosphate 5 phosphatase SIP-110 mRNA, complete cds	4296	4297G>A	3
		GEN- 33X			Human lymphocyte specific interferon regulatory factor/interferon regulatory factor 4 (LSIRF/IRF4) mRNA, complete cds	4680	4681T>G	3
		GEN- 33X			Human lymphocyte specific interferon regulatory factor/interferon regulatory factor 4 (LSIRF/IRF4) mRNA, complete cds	4732	4733T>G	3
		GEN- 33X			Human lymphocyte specific interferon regulatory factor/interferon regulatory factor 4 (LSIRF/IRF4) mRNA, complete cds	4942	4943A>G	3
		GEN- 33X			Human lymphocyte specific interferon regulatory factor/interferon regulatory factor 4 (LSIRF/IRF4) mRNA, complete cds	5079	5080T>C	3
		GEN- 35Z			Homo sapiens human gamma-glutamyl hydrolase (hGH) mRNA, complete cds	75	16T>C	C6R
		GEN- 35Z			Homo sapiens human gamma-glutamyl hydrolase (hGH) mRNA, complete cds	150	91G>A	A31T
		GEN-			Homo sapiens human cds	511	452C>T	T151I

U55206	U55206	None	GEN-35Z	35Z gamma-glutamyl hydrolase (hGH) mRNA, complete cds	1161	1102A>G	3
U56390	U56390	602234	GEN-36X	Homo sapiens human gamma-glutamyl hydrolase (hGH) mRNA, complete cds	411	408C>T	S
U58196	U58196	147685	GEN-67	Human cysteine protease ICE-LAP6 mRNA, complete cds	2711	2514A>G	3
U59863	U59863	None	GEN-3A7	INTERLEUKIN ENHANCER-BINDING FACTOR Human TRAF-interacting protein I-TRAF mRNA, complete cds	367	209A>G	D70G
U59863	U59863	None	GEN-3A7	Human TRAF-interacting protein I-TRAF mRNA, complete cds	1863	1705A>T	3
U59863	U59863	None	GEN-3A7	Human TRAF-interacting protein I-TRAF mRNA, complete cds	2046	1888G>A	3
U60519	U60519	601762	GEN-3AZ	Human apoptotic cysteine protease Mch4 (Mch4) mRNA, complete cds	304	157G>A	E53K
U60519	U60519	601762	GEN-3AZ	Human apoptotic cysteine protease Mch4 (Mch4) mRNA, complete cds	324	177A>G	S
U60800	U60800	None	GEN-3BC	Human semaphorin (CD100) mRNA, complete cds	779	692T>G	V231G
U61849	U61849	602367	GEN-3C0	Human neuronal pentraxin 1 (NPTX1) mRNA, complete cds	4963	4825T>C	3
CHRNA2	U62431	118502	GEN-4EN	Nicotinic, Cholinergic receptor alpha 2	2296	1742C>G	3
CHRNA2	U62431	118502	GEN-4EN	Nicotinic, Cholinergic receptor alpha 2	2387	1833C>T	3
CHRNA2	U62431	118502	GEN-4EN	Nicotinic, Cholinergic receptor alpha 2	2504	1950G>T	3
CHRNA2	U62431	118502	GEN-4EN	Nicotinic, Cholinergic receptor alpha 2	2538	1984G>A	3

U62433	U62433	118504	4EN GEN-4P	receptor alpha 2 Nicotinic, Cholinergic	870	639C>T	S
U62433	U62433	118504	GEN-4P	receptor alpha 4 Nicotinic, Cholinergic	870	639C>T	S
U62433	U62433	118504	GEN-4P	receptor alpha 4 Nicotinic, Cholinergic	909	678C>T	S
U62433	U62433	118504	GEN-4P	receptor alpha 4 Nicotinic, Cholinergic	909	678C>T	S
U62433	U62433	118504	GEN-4P	receptor alpha 4 Nicotinic, Cholinergic	1440	1209T>G	S
U62433	U62433	118504	GEN-4P	receptor alpha 4 Nicotinic, Cholinergic	1440	1209T>G	S
U62433	U62433	118504	GEN-4P	receptor alpha 4 Nicotinic, Cholinergic	1458	1227C>T	S
U62433	U62433	118504	GEN-4P	receptor alpha 4 Nicotinic, Cholinergic	1584	1353G>A	S
U62433	U62433	118504	GEN-4P	receptor alpha 4 Nicotinic, Cholinergic	1781	1550C>T	S517L
U62433	U62433	118504	GEN-4P	receptor alpha 4 Nicotinic, Cholinergic	1860	1629C>T	S
U62433	U62433	118504	GEN-4P	receptor alpha 4 Nicotinic, Cholinergic	1860	1629C>T	S
U62433	U62433	118504	GEN-4P	receptor alpha 4 Nicotinic, Cholinergic	1890	1659G>A	S
U62433	U62433	118504	GEN-4P	receptor alpha 4 Nicotinic, Cholinergic	1890	1659G>A	S
U70321	U70321	None	GEN- 3K9	Human herpesvirus entry mediator mRNA, complete cds	343	50G>A	R17K
U70321	U70321	None	GEN- 3K9	Human herpesvirus entry mediator mRNA, complete cds	1014	721G>A	V241I
U70321	U70321	None	GEN- 3K9	Human herpesvirus entry mediator mRNA, complete cds	1218	925A>G	3
U70321	U70321	None	GEN- 3K9	Human herpesvirus entry mediator mRNA, complete cds	1249	956C>T	3
U70321	U70321	None	GEN- 3K9	Human herpesvirus entry mediator mRNA, complete cds	1453	1160G>A	3

U70451	U70451	602170	GEN-3KB	cds Human myeloid differentiation primary response protein MyD88 mRNA, complete cds	2167	2135A>G	3
U70451	U70451	602170	GEN-3KB	Human myeloid differentiation primary response protein MyD88 mRNA, complete cds	2516	2484A>G	3
U71321	U71321	602623	GEN-2TW	Human FK506-binding protein FKBP51 mRNA, complete cds	1248	1095C>T	S
U71321	U71321	602623	GEN-2TW	Human FK506-binding protein FKBP51 mRNA, complete cds	1425	1272G>A	S
U73338	U73338	156570	GEN-69	Methionine Synthase	1158	764G>A	C255Y
U73338	U73338	156570	GEN-69	Methionine Synthase	5095	4701G>A	3
U73338	U73338	156570	GEN-69	Methionine Synthase	6750	6356G>A	3
U75283	U75283	None	GEN-3NV	Human sigma receptor mRNA, complete cds	251	204G>A	S
U75283	U75283	None	GEN-3NV	Human sigma receptor mRNA, complete cds	1625	1578A>C	3
U78294	U78294	603697	GEN-3QZ	Homo sapiens 15S-lipoxygenase mRNA, complete cds	2449	2378A>G	3
U81375	U81375	602193	GEN-3VO	Human placental equilibrative nucleoside transporter 1 (hENT1) mRNA, complete cds	1989	1811G>A	3
U81375	U81375	602193	GEN-3VO	Human placental equilibrative nucleoside transporter 1 (hENT1) mRNA, complete cds	1996	1818C>T	3
U81375	U81375	602193	GEN-3VO	Human placental equilibrative nucleoside transporter 1 (hENT1) mRNA, complete cds	2045	1867T>C	3
U84487	U84487	601880	GEN-3ZJ	Human CX3C chemokine precursor, mRNA, alternatively spliced, complete cds	3015	2936T>C	3

U84487	U84487	601880	GEN-3ZJ	Human CX3C chemokine precursor, mRNA, alternatively spliced, complete cds	3058	2979T>C	3
U86358	U86358	602565	GEN-LR6	Human chemokine (TECK) mRNA, complete cds	378	378A>G	S
CD39	U87967	601752	GEN-44L	Human ATP diphosphohydrolase mRNA, complete cds	1233	1203C>T	S
V00537	V00537	147578	GEN-U1	Interferon alpha 13	40	(-17)T>C	5
V00537	V00537	147578	GEN-U1	Interferon alpha 13	55	(-2)C>T	5
V00537	V00537	147578	GEN-U1	Interferon alpha 13	466	410C>T	A137V
V00537	V00537	147578	GEN-U1	Interferon alpha 13	808	752G>A	3
IFNA14	V00542	147579	GEN-TT	Interferon alpha 14	47	(-10)G>A	5
IFNA14	V00542	147579	GEN-TT	Interferon alpha 14	50	(-7)A>G	5
IFNA14	V00542	147579	GEN-TT	Interferon alpha 14	579	523T>C	F175L
IFNA14	V00542	147579	GEN-TT	Interferon alpha 14	630	574C>G	3
IFNA14	V00542	147579	GEN-TT	Interferon alpha 14	740	684C>T	3
IFNA14	V00542	147579	GEN-TT	Interferon alpha 14	760	704T>A	3
IFNA14	V00542	147579	GEN-TT	Interferon alpha 14	771	715G>A	3
IFNA14	V00542	147579	GEN-TT	Interferon alpha 14	775	719T>A	3
IFNA14	V00542	147579	GEN-TT	Interferon alpha 14	812	756T>G	3
IFNA14	V00542	147579	GEN-TT	Interferon alpha 14	898	842A>T	3
IFNA14	V00542	147579	GEN-TT	Interferon alpha 14	921	865G>A	3
IFNB1	V00546	147640	GEN-TV	Messenger RNA for human fibroblast interferon	474	410T>G	L137R
V00548	V00548	147562	GEN-P2	Human messenger RNA for leukocyte (alpha-2) interferon	119	119G>A	R40K
IFNA10	V00551	147577	GEN-TS	Interferon alpha 7	462	416C>T	S139F
IFNA10	V00551	147577	GEN-TS	Interferon alpha 7	510	464T>C	I155T
IFNA10	V00551	147577	GEN-TS	Interferon alpha 7	516	470G>A	R157K
IFNA10	V00551	147577	GEN-TS	Interferon alpha 7	712	666G>C	3
IFNA10	V00551	147577	GEN-TS	Interferon alpha 7	716	670C>T	3
V00567	V00567	109700	GEN-P3	Human messenger RNA fragment for the beta-2 microglobulin	303	303C>A	S
HLA-	X00033	146880	GEN-T0	Human RNA sequence of	41	22A>C	M8L

[illegible]

HLA-DQA1	X00033	146880	GEN-T0	Human RNA sequence of the human DS glycoprotein alpha subunit from the HLA-D region of the major histocompatibility complex(MHC)	243	224A>G	H75R
HLA-DQA1	X00033	146880	GEN-T0	Human RNA sequence of the human DS glycoprotein alpha subunit from the HLA-D region of the major histocompatibility complex(MHC)	248	229C>T	L77F
HLA-DQA1	X00033	146880	GEN-T0	Human RNA sequence of the human DS glycoprotein alpha subunit from the HLA-D region of the major histocompatibility complex(MHC)	298	279T>C	S
HLA-DQA1	X00033	146880	GEN-T0	Human RNA sequence of the human DS glycoprotein alpha subunit from the HLA-D region of the major histocompatibility complex(MHC)	311	292C>G	L98V
HLA-DQA1	X00033	146880	GEN-T0	Human RNA sequence of the human DS glycoprotein alpha subunit from the HLA-D region of the major histocompatibility complex(MHC)	334	315C>T	S
HLA-DQA1	X00033	146880	GEN-T0	Human RNA sequence of the human DS glycoprotein alpha subunit from the HLA-D region of the major histocompatibility complex(MHC)	388	369A>G	S
HLA-DQA1	X00033	146880	GEN-T0	Human RNA sequence of the human DS glycoprotein alpha subunit from the HLA-D region of the major histocompatibility complex(MHC)	559	540T>G	S

HLA-DQA1	X00033	146880	GEN-T0	Human RNA sequence of the human DS glycoprotein alpha subunit from the HLA-D region of the major histocompatibility complex(MHC)	564	545C>A	A182D
HLA-DQA1	X00033	146880	GEN-T0	Human RNA sequence of the human DS glycoprotein alpha subunit from the HLA-D region of the major histocompatibility complex(MHC)	607	588T>C	S
HLA-DQA1	X00033	146880	GEN-T0	Human RNA sequence of the human DS glycoprotein alpha subunit from the HLA-D region of the major histocompatibility complex(MHC)	644	625G>A	A209T
HLA-DQA1	X00033	146880	GEN-T0	Human RNA sequence of the human DS glycoprotein alpha subunit from the HLA-D region of the major histocompatibility complex(MHC)	646	627A>C	S
HLA-DQA1	X00033	146880	GEN-T0	Human RNA sequence of the human DS glycoprotein alpha subunit from the HLA-D region of the major histocompatibility complex(MHC)	679	660T>C	S
HLA-DQA1	X00033	146880	GEN-T0	Human RNA sequence of the human DS glycoprotein alpha subunit from the HLA-D region of the major histocompatibility complex(MHC)	688	669G>A	S
HLA-DQA1	X00033	146880	GEN-T0	Human RNA sequence of the human DS glycoprotein alpha subunit from the HLA-D region of the major histocompatibility complex(MHC)	704	685G>A	V229M

HLA-DQA1	X00033	146880	GEN-T0	Human RNA sequence of the human DS glycoprotein alpha subunit from the HLA-D region of the major histocompatibility complex(MHC)	721	702G>C	S
HLA-DQA1	X00033	146880	GEN-T0	Human RNA sequence of the human DS glycoprotein alpha subunit from the HLA-D region of the major histocompatibility complex(MHC)	724	705C>T	S
HLA-DQA1	X00033	146880	GEN-T0	Human RNA sequence of the human DS glycoprotein alpha subunit from the HLA-D region of the major histocompatibility complex(MHC)	730	711G>C	L237F
HLA-DQA1	X00033	146880	GEN-T0	Human RNA sequence of the human DS glycoprotein alpha subunit from the HLA-D region of the major histocompatibility complex(MHC)	800	781A>G	3
X00497	X00497	142790	GEN-TN	Human mRNA for HLA-DR antigens associated invariant chain (p33)	805	750A>G	3
X00497	X00497	142790	GEN-TN	Human mRNA for HLA-DR antigens associated invariant chain (p33)	881	826A>G	3
X00497	X00497	142790	GEN-TN	Human mRNA for HLA-DR antigens associated invariant chain (p33)	1144	1089C>G	3
HLA-DPB1	X00532	142858	GEN-U2	Human mRNA for SB beta-chain (clone pII-beta-7)	13	13T>A	S5T
HLA-DPB1	X00532	142858	GEN-U2	Human mRNA for SB beta-chain (clone pII-beta-7)	91	91T>A	S31T
HLA-DPB1	X00532	142858	GEN-U2	Human mRNA for SB beta-chain (clone pII-beta-7)	94	94C>T	R32C

HLA-DPB1	X00532	142858	GEN-U2	Human mRNA for SB beta-chain (clone pII-beta-7)	151	151C>A	L51M
HLA-DPB1	X00532	142858	GEN-U2	Human mRNA for SB beta-chain (clone pII-beta-7)	154	154C>A	S
HLA-DPB1	X00532	142858	GEN-U2	Human mRNA for SB beta-chain (clone pII-beta-7)	158	158G>C	S53T
HLA-DPB1	X00532	142858	GEN-U2	Human mRNA for SB beta-chain (clone pII-beta-7)	213	213G>A	S
HLA-DPB1	X00532	142858	GEN-U2	Human mRNA for SB beta-chain (clone pII-beta-7)	281	281C>T	T94M
HLA-DPB1	X00532	142858	GEN-U2	Human mRNA for SB beta-chain (clone pII-beta-7)	306	306C>T	S
HLA-DPB1	X00532	142858	GEN-U2	Human mRNA for SB beta-chain (clone pII-beta-7)	341	341A>G	Q114R
HLA-DPB1	X00532	142858	GEN-U2	Human mRNA for SB beta-chain (clone pII-beta-7)	353	353G>A	R118Q
HLA-DPB1	X00532	142858	GEN-U2	Human mRNA for SB beta-chain (clone pII-beta-7)	488	488C>T	T163M
HLA-DPB1	X00532	142858	GEN-U2	Human mRNA for SB beta-chain (clone pII-beta-7)	496	496T>C	S166P
HLA-DPB1	X00532	142858	GEN-U2	Human mRNA for SB beta-chain (clone pII-beta-7)	524	524C>T	T175I
HLA-DPB1	X00532	142858	GEN-U2	Human mRNA for SB beta-chain (clone pII-beta-7)	568	568A>G	R190G
HLA-DPB1	X00532	142858	GEN-U2	Human mRNA for SB beta-chain (clone pII-beta-7)	600	600G>A	S
HLA-DPB1	X00532	142858	GEN-U2	Human mRNA for SB beta-chain (clone pII-beta-7)	708	708C>G	F
HLA-DPB1	X00532	142858	GEN-U2	Human mRNA for SB beta-chain (clone pII-beta-7)	761	761G>A	3
HLA-DPB1	X00532	142858	GEN-U2	Human mRNA for SB beta-chain (clone pII-beta-7)	840	840G>A	3
EGFR	X00663	131550	GEN-U4	Human mRNA fragment for epidermal growth factor (EGF) receptor	1136	1136G>A	R379K
EGFR	X00663	131550	GEN-U4	Human mRNA fragment for epidermal growth factor (EGF) receptor	1935	1935A>G	S
EGFR	X00663	131550	GEN-U4	Human mRNA fragment for epidermal growth factor (EGF) receptor	2283	2283C>T	S

X00734	X00734	None	GEN-MST	Human beta-tubulin gene (5-beta) with ten Alu family members	1059	1059G>T	S
X00737	X00737	164050	GEN-P8	Human mRNA for purine nucleoside phosphorylase (PNP; EC 2.4.2.1)	59	(-51)T>G	5
X00737	X00737	164050	GEN-P8	Human mRNA for purine nucleoside phosphorylase (PNP; EC 2.4.2.1)	169	60T>C	S
X00737	X00737	164050	GEN-P8	Human mRNA for purine nucleoside phosphorylase (PNP; EC 2.4.2.1)	260	151A>G	S51G
X00737	X00737	164050	GEN-P8	Human mRNA for purine nucleoside phosphorylase (PNP; EC 2.4.2.1)	280	171T>C	S
X00737	X00737	164050	GEN-P8	Human mRNA for purine nucleoside phosphorylase (PNP; EC 2.4.2.1)	1254	1145G>A	3
X01394	X01394	191160	GEN-4Y	Tumor necrosis factor	125	(-28)C>T	5
X01586	X01586	147680	GEN-PC	Interleukin 2	332	225T>G	H75Q
X01586	X01586	147680	GEN-PC	Interleukin 2	563	456G>A	S
X02317	X02317	147450	GEN-KM	Superoxide dismutase 1 (Cu/Zn)	614	550A>C	3
X02469	X02469	191170	GEN-PF	Human mRNA for p53 cellular tumor antigen	350	215C>G	P72R
X02469	X02469	191170	GEN-PF	Human mRNA for p53 cellular tumor antigen	953	818G>A	R273H
X02492	X02492	147572	GEN-1T	Interferon alpha inducible protein	415	346C>G	R116G
X02492	X02492	147572	GEN-1T	Interferon alpha inducible protein	417	348G>C	S
X02598	X02598	305370	GEN-X6	Human mRNA for EPA glycoprotein (erythroid-potentiating activity)	64	23C>T	A8V
X02598	X02598	305370	GEN-X6	Human mRNA for EPA glycoprotein (erythroid-potentiating activity)	108	67C>G	P23A
X02598	X02598	305370	GEN-X6	Human mRNA for EPA glycoprotein (erythroid-potentiating activity)	298	257C>A	T86N
X02598	X02598	305370	GEN-X6	Human mRNA for EPA glycoprotein (erythroid-potentiating activity)	413	372T>C	S

X02812	X02812	190180	GEN-XR	glycoprotein (erythroid- potentiating activity)	870	29C>T	P10L
X02812	X02812	190180	GEN-XR	Human mRNA for transforming growth factor- beta (TGF-beta)	979	138C>G	I46M
X02812	X02812	190180	GEN-XR	Human mRNA for transforming growth factor- beta (TGF-beta)	1632	791C>T	T264I
X02812	X02812	190180	GEN-XR	Human mRNA for transforming growth factor- beta (TGF-beta)	1807	966C>T	S
X02812	X02812	190180	GEN-XR	Human mRNA for transforming growth factor- beta (TGF-beta)	1930	1089G>A	S
X02812	X02812	190180	GEN-XR	Human mRNA for transforming growth factor- beta (TGF-beta)	1942	1101C>T	S
X02812	X02812	190180	GEN-XR	Human mRNA for transforming growth factor- beta (TGF-beta)	2013	1172G>A	S391N
HLA-DOB	X03066	600629	GEN-ZG	Human mRNA for HLA-D class II antigen DO beta chain	32	(-25)G>A	5
HLA-DOB	X03066	600629	GEN-ZG	Human mRNA for HLA-D class II antigen DO beta chain	1147	1091C>T	3
HLA-DOB	X03066	600629	GEN-ZG	Human mRNA for HLA-D class II antigen DO beta chain	1299	1243A>G	3
X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	79	(-3)A>G	5
X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	97	16T>G	S6A
X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	203	122A>T	Y41F

X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	318	237C>T	S
X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	408	327G>A	S
X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	523	442A>G	I148V
X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	550	469A>G	S157G
X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	566	485G>A	R162Q
X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	597	516C>T	S
X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	618	537C>T	S
X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	627	546C>T	S
X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	639	558C>T	S
X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	677	596G>A	R199H
X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	684	603T>C	S
X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	767	686G>A	S229N
X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	784	703G>A	V235I
X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	816	735T>C	S

X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	822	741T>G	S
X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	848	767G>A	R256Q
X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	879	798G>A	3
X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	889	808A>G	3
X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	892	811C>T	3
X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	924	843C>G	3
X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	998	917A>G	3
X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	1073	992A>T	3
X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	1082	1001A>G	3
X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	1095	1014C>T	3
X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	1107	1026C>T	3
X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	1117	1036A>T	3
X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	1128	1047G>A	3
X03068	X03068	142857	GEN-ZH	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	1133	1052C>T	3

X03068	X03068	142857	GEN-ZH	class II antigen DQw1.1 beta chain	1180	1099C>T	3
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DQw1.1 beta chain	99	37A>G	T13A
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	104	42G>T	S
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	348	286C>A	L96I
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	361	299G>A	R100K
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	452	390G>A	S
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	459	397T>G	S133A
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	463	401A>G	K134R
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	471	409C>A	P137T
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	500	438C>T	S
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	508	446G>A	S149N
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	523	461G>C	G154A
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	547	485G>T	R162L

X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	551	489C>T	S
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	552	490G>A	G164S
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	567	505G>A	A169T
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	573	511G>A	V171M
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	584	522A>G	S
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	593	531C>T	S
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	596	534G>C	Q178H
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	605	543T>C	S
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	632	570G>A	S
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	647	585G>A	S
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	686	624T>C	S
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	691	629C>T	T210M
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	692	630G>A	S
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	716	654A>T	R218S

X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	721	659G>A	R220Q
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	756	694G>A	V232I
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	767	705C>T	S
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	800	738G>A	S
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	814	752G>A	R251K
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	847	785C>G	T262R
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	865	803A>G	3
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	868	806C>A	3
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	893	831C>T	3
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	899	837T>C	3
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	903	841A>G	3
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	913	851A>G	3
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	988	926G>A	3
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	1004	942G>A	3

X03069	X03069	142857	GEN-PI	class II antigen DR1 beta chain	1027	965C>T	3
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	1105	1043G>C	3
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	1128	1066C>T	3
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	1139	1077C>T	3
X03069	X03069	142857	GEN-PI	Human mRNA for HLA-D class II antigen DR1 beta chain	1140	1078G>C	3
X03438	X03438	138970	GEN-PM	Human mRNA for granulocyte colony-stimulating factor (G-CSF)	586	555G>A	S
X03438	X03438	138970	GEN-PM	Human mRNA for granulocyte colony-stimulating factor (G-CSF)	1235	1204C>T	3
X03663	X03663	164770	GEN-51	Colony stimulating factor 1 receptor	3732	3432T>C	3
X03663	X03663	164770	GEN-51	Colony stimulating factor 1 receptor	3951	3651C>A	3
X03674	X03674	305900	GEN-9K	Glucose-6-phosphate dehydrogenase	503	33C>G	H11Q
X03674	X03674	305900	GEN-9K	Glucose-6-phosphate dehydrogenase	589	119C>T	S40L
X03674	X03674	305900	GEN-9K	Glucose-6-phosphate dehydrogenase	672	202G>A	V68M
X03674	X03674	305900	GEN-9K	Glucose-6-phosphate dehydrogenase	846	376A>G	N126D
X03674	X03674	305900	GEN-9K	Glucose-6-phosphate dehydrogenase	2215	1745T>C	3
X03674	X03674	305900	GEN-9K	Glucose-6-phosphate dehydrogenase	2242	1772T>C	3
X03674	X03674	305900	GEN-9K	Glucose-6-phosphate dehydrogenase	2341	1871G>A	3

X03884	X03884	186830	GEN-52	CD3E antigen, epsilon polypeptide (TiT3 complex)	108	54C>T	S
X03884	X03884	186830	GEN-52	CD3E antigen, epsilon polypeptide (TiT3 complex)	1258	1204T>A	3
X04391	X04391	None	GEN-14D	Human mRNA for lymphocyte glycoprotein T1/Leu-1	2084	2012G>A	3
CD1A	X04450	188370	GEN-14J	Human CD1 mRNA fragment for HTA1 thymocyte antigen (3terminal fragment)	402	402T>C	S
X04476	X04476	153390	GEN-14K	Human mRNA fragment for p56(LSTRA) protein-tyrosine kinase	601	601G>A	3
X04571	X04571	131530	GEN-KY0	Human mRNA for kidney epidermal growth factor (EGF) precursor	4507	4071G>A	3
X04608	X04608	104770	GEN-PQ	Human mRNA for serum amyloid P component (SAP)	698	602T>C	I201T
X06180	X06180	186820	GEN-19A	Human mRNA for CD7 antigen (gp40)	1121	1122C>T	3
ITGA5	X06256	135620	GEN-19B	Human mRNA for fibronectin receptor alpha subunit	2562	2539C>A	L847I
X06318	X06318	176970	GEN-KY	Protein kinase C, beta 1	83	(-54)G>C	5
X06318	X06318	176970	GEN-KY	Protein kinase C, beta 1	940	804G>A	S
X06318	X06318	176970	GEN-KY	Protein kinase C, beta 1	1327	1191T>C	S
X06318	X06318	176970	GEN-KY	Protein kinase C, beta 1	1906	1770C>T	S
TCRD	X06557	186810	GEN-19M	Human mRNA for TCR-delta chain	1032	1014C>A	3
X07523	X07523	134371	GEN-1E5	Human mRNA for truncated form of complement factor H	1170	1097G>A	G366E
X07523	X07523	134371	GEN-1E5	Human mRNA for truncated form of complement factor H	1277	1204T>C	Y402H
SOD2	X07834	147460	GEN-1ES	Human mRNA for manganese superoxide dismutase (EC 1.15.1.1)	44	40C>G	P14A

SOD2	X07834	147460	GEN-1ES	Human mRNA for manganese superoxide dismutase (EC 1.15.1.1)	51	47T>C	V16A
SOD2	X07834	147460	GEN-1ES	Human mRNA for manganese superoxide dismutase (EC 1.15.1.1)	198	194C>A	T65N
SOD2	X07834	147460	GEN-1ES	Human mRNA for manganese superoxide dismutase (EC 1.15.1.1)	249	245T>C	I82T
ITGB1	X07979	135630	GEN-4E5	Human mRNA for fibronectin receptor beta subunit	1189	1086A>C	S
ITGB1	X07979	135630	GEN-4E5	Human mRNA for fibronectin receptor beta subunit	1279	1176A>C	S
ITGB1	X07979	135630	GEN-4E5	Human mRNA for fibronectin receptor beta subunit	2713	2610T>C	3
ITGB1	X07979	135630	GEN-4E5	Human mRNA for fibronectin receptor beta subunit	2878	2775T>A	3
ITGB1	X07979	135630	GEN-4E5	Human mRNA for fibronectin receptor beta subunit	3339	3236A>G	3
ITGB1	X07979	135630	GEN-4E5	Human mRNA for fibronectin receptor beta subunit	3531	3428G>A	3
ANX5	X12454	131230	GEN-1M2	Human mRNA for vascular anticoagulant	128	(-1)C>T	5
ANX5	X12454	131230	GEN-1M2	Human mRNA for vascular anticoagulant	1413	1285T>G	3
ANX5	X12454	131230	GEN-1M2	Human mRNA for vascular anticoagulant	1431	1303C>T	3
ANX5	X12454	131230	GEN-1M2	Human mRNA for vascular anticoagulant	1518	1390G>A	3
X12530	X12530	112210	GEN-1MH	Human mRNA for B lymphocyte antigen CD20 (B1, Bp35)	131	38C>T	P13L
X12530	X12530	112210	GEN-1MH	Human mRNA for B lymphocyte antigen CD20 (B1, Bp35)	1318	1225G>A	3

X13403	X13403	164175	GEN-L8	POU domain, class 2, transcription factor 1	1298	1239T>C	S
X13403	X13403	164175	GEN-L8	POU domain, class 2, transcription factor 1	1476	1417G>A	A473T
X13561	X13561	147910	GEN-10H	Human mRNA for preprokallikrein (EC 3.4.21)	54	18G>T	S
X13561	X13561	147910	GEN-10H	Human mRNA for preprokallikrein (EC 3.4.21)	441	405T>C	S
X13561	X13561	147910	GEN-10H	Human mRNA for preprokallikrein (EC 3.4.21)	469	433G>C	E145Q
X13561	X13561	147910	GEN-10H	Human mRNA for preprokallikrein (EC 3.4.21)	592	556A>G	K186E
LIF	X13967	159540	GEN-1PZ	Human mRNA for leukaemia inhibitory factor (LIF/HILDA)	3710	3666T>G	3
X14356	X14356	146760	GEN-1R0	Human mRNA for high affinity Fc receptor (FcRI)	195	159T>C	S
X14356	X14356	146760	GEN-1R0	Human mRNA for high affinity Fc receptor (FcRI)	1006	970G>A	D324N
X14356	X14356	146760	GEN-1R0	Human mRNA for high affinity Fc receptor (FcRI)	1161	1125G>A	S
X14356	X14356	146760	GEN-1R0	Human mRNA for high affinity Fc receptor (FcRI)	1164	1128G>A	3
X14356	X14356	146760	GEN-1R0	Human mRNA for high affinity Fc receptor (FcRI)	1174	1138G>T	3
X14356	X14356	146760	GEN-1R0	Human mRNA for high affinity Fc receptor (FcRI)	1203	1167C>T	3
X14356	X14356	146760	GEN-1R0	Human mRNA for high affinity Fc receptor (FcRI)	1217	1181G>A	3
X14356	X14356	146760	GEN-1R0	Human mRNA for high affinity Fc receptor (FcRI)	1279	1243G>A	3
X14583	X14583	None	GEN-1R0	Human mRNA for Ig lambda-chain	131	107A>G	K36R
X14583	X14583	None	GEN-1R0	Human mRNA for Ig lambda-chain	132	108G>A	S
X14583	X14583	None	GEN-1R0	Human mRNA for Ig lambda-chain	164	140A>C	N47T
X14583	X14583	None	GEN-1R0	Human mRNA for Ig lambda-chain	255	231G>T	S
X14583	X14583	None	GEN-1R0	Human mRNA for Ig lambda-chain	381	357A>G	S

X14583	X14583	None	GEN-1RJ	Human mRNA for Ig lambda-chain	400	376C>G	L126V
X14583	X14583	None	GEN-1RJ	Human mRNA for Ig lambda-chain	412	388G>A	G130S
X14583	X14583	None	GEN-1RJ	Human mRNA for Ig lambda-chain	450	426G>A	S
X14583	X14583	None	GEN-1RJ	Human mRNA for Ig lambda-chain	522	498C>T	S
X14583	X14583	None	GEN-1RJ	Human mRNA for Ig lambda-chain	540	516G>C	K172N
X14583	X14583	None	GEN-1RJ	Human mRNA for Ig lambda-chain	553	529C>A	P177T
X14583	X14583	None	GEN-1RJ	Human mRNA for Ig lambda-chain	594	570A>G	S
X14583	X14583	None	GEN-1RJ	Human mRNA for Ig lambda-chain	624	600T>C	S
X14583	X14583	None	GEN-1RJ	Human mRNA for Ig lambda-chain	639	615T>C	S
X14583	X14583	None	GEN-1RJ	Human mRNA for Ig lambda-chain	659	635G>A	R212K
X14583	X14583	None	GEN-1RJ	Human mRNA for Ig lambda-chain	738	714A>C	3
X14583	X14583	None	GEN-1RJ	Human mRNA for Ig lambda-chain	740	716A>T	3
X14583	X14583	None	GEN-1RJ	Human mRNA for Ig lambda-chain	752	728C>A	3
X14583	X14583	None	GEN-1RJ	Human mRNA for Ig lambda-chain	858	834C>G	3
CHRNA1	X14830	100710	GEN-1RJ	Human mRNA for Ig lambda-chain	1375	1359C>T	S
CHRNA1	X14830	100710	GEN-4EK	Nicotinic, Cholinergic receptor beta 1	1591	1575T>C	3
X15263	X15263	None	GEN-4EK	Nicotinic, Cholinergic receptor beta 1	1144	1044G>A	S
X15606	X15606	146630	GEN-4EQ	Muscarinic receptor, CHRM1	884	822G>A	S
IRF2	X15949	147576	GEN-1UO	Intercellular adhesion molecule 2	842	744G>A	S
X16166	X16166	182284	GEN-QT	Human mRNA for interferon regulatory factor-2 (IRF-2)	41	(-12)T>G	5
				Human mRNA for putative cytokine 21 (HC21)			

X16166	X16166	182284	GEN-QT	Human mRNA for putative cytokine 21 (HC21)	86	34A>G	M12V
X16166	X16166	182284	GEN-QT	Human mRNA for putative cytokine 21 (HC21)	111	59C>T	P20L
X16166	X16166	182284	GEN-QT	Human mRNA for putative cytokine 21 (HC21)	115	63G>A	S
X16166	X16166	182284	GEN-QT	Human mRNA for putative cytokine 21 (HC21)	162	110C>T	S37F
X16166	X16166	182284	GEN-QT	Human mRNA for putative cytokine 21 (HC21)	260	208A>G	S70G
X16166	X16166	182284	GEN-QT	Human mRNA for putative cytokine 21 (HC21)	274	222T>C	S
X16166	X16166	182284	GEN-QT	Human mRNA for putative cytokine 21 (HC21)	280	228T>C	S
X16166	X16166	182284	GEN-QT	Human mRNA for putative cytokine 21 (HC21)	289	237A>G	S
X16166	X16166	182284	GEN-QT	Human mRNA for putative cytokine 21 (HC21)	375	323C>T	3
X16166	X16166	182284	GEN-QT	Human mRNA for putative cytokine 21 (HC21)	393	341A>C	3
X16166	X16166	182284	GEN-QT	Human mRNA for putative cytokine 21 (HC21)	395	343A>G	3
X16166	X16166	182284	GEN-QT	Human mRNA for putative cytokine 21 (HC21)	437	385C>T	3
X16166	X16166	182284	GEN-QT	Human mRNA for putative cytokine 21 (HC21)	549	497G>C	3
CSNK2B	X16312	115441	GEN-1XW	Human mRNA for cytokine 21 (HC21)	271	138T>C	S
CSNK2B	X16312	115441	GEN-1XW	Human mRNA for phosphatase/casein kinase II beta subunit	812	679A>T	3
CSNK2B	X16312	115441	GEN-1XW	Human mRNA for phosphatase/casein kinase II beta subunit	885	752T>C	3
X16863	X16863	146740	GEN-1YV	Human Fc-gamma RIII-1 cDNA for Fc-gamma receptor III-1 (CD 16)	141	108C>G	S36R
X16863	X16863	146740	GEN-1YV	Human Fc-gamma RIII-1 cDNA for Fc-gamma receptor III-1 (CD 16)	147	114T>C	S

X16863	X16863	146740	GEN-1YV	Human Fc-gamma RIII-1 cDNA for Fc-gamma receptor III-1 (CD 16)	277	244A>G	N82D
X16863	X16863	146740	GEN-1YV	Human Fc-gamma RIII-1 cDNA for Fc-gamma receptor III-1 (CD 16)	473	440A>G	D147G
X16863	X16863	146740	GEN-1YV	Human Fc-gamma RIII-1 cDNA for Fc-gamma receptor III-1 (CD 16)	505	472C>T	H158Y
X16863	X16863	146740	GEN-1YV	Human Fc-gamma RIII-1 cDNA for Fc-gamma receptor III-1 (CD 16)	531	498T>C	S
X16863	X16863	146740	GEN-1YV	Human Fc-gamma RIII-1 cDNA for Fc-gamma receptor III-1 (CD 16)	559	526G>T	V176F
X16863	X16863	146740	GEN-1YV	Human Fc-gamma RIII-1 cDNA for Fc-gamma receptor III-1 (CD 16)	733	700T>C	F
X16863	X16863	146740	GEN-1YV	Human Fc-gamma RIII-1 cDNA for Fc-gamma receptor III-1 (CD 16)	766	733C>T	3
X16863	X16863	146740	GEN-1YV	Human Fc-gamma RIII-1 cDNA for Fc-gamma receptor III-1 (CD 16)	829	796G>A	3
MIC2	X16996	313470	GEN-1ZE	Human mRNA for T-cell surface glycoprotein E2	210	87T>C	S
MIC2	X16996	313470	GEN-1ZE	Human mRNA for T-cell surface glycoprotein E2	283	160G>A	D54N
MIC2	X16996	313470	GEN-1ZE	Human mRNA for T-cell surface glycoprotein E2	486	363C>T	S
MIC2	X16996	313470	GEN-1ZE	Human mRNA for T-cell surface glycoprotein E2	1068	945C>T	3
X17033	X17033	192974	GEN-LG	Integrin, alpha 2 (CD49B, alpha 2 subunit of VLA-2 receptor)	4193	4145T>G	3
X17033	X17033	192974	GEN-LG	Integrin, alpha 2 (CD49B, alpha 2 subunit of VLA-2 receptor)	4849	4801A>G	3
X17033	X17033	192974	GEN-LG	Integrin, alpha 2 (CD49B, alpha 2 subunit of VLA-2 receptor)	4897	4849A>G	3

X17042	X17042	177040	GEN-1ZN	Human mRNA for hematopoietic proteoglycan core protein	324	300C>T	S
X17042	X17042	177040	GEN-1ZN	Human mRNA for hematopoietic proteoglycan core protein	1021	997G>T	3
IGHM	X17115	147020	GEN-1ZX	Human mRNA for IgM heavy chain complete sequence	849	777T>C	S
IGHM	X17115	147020	GEN-1ZX	Human mRNA for IgM heavy chain complete sequence	1102	1030A>G	S344G
IGHM	X17115	147020	GEN-1ZX	Human mRNA for IgM heavy chain complete sequence	1107	1035G>A	S
IGHM	X17115	147020	GEN-1ZX	Human mRNA for IgM heavy chain complete sequence	1175	1103T>G	V368G
IGHM	X17115	147020	GEN-1ZX	Human mRNA for IgM heavy chain complete sequence	1212	1140C>T	S
IGHM	X17115	147020	GEN-1ZX	Human mRNA for IgM heavy chain complete sequence	1561	1489C>G	R497G
IGHM	X17115	147020	GEN-1ZX	Human mRNA for IgM heavy chain complete sequence	1692	1620G>T	Q540H
IGHM	X17115	147020	GEN-1ZX	Human mRNA for IgM heavy chain complete sequence	1816	1744G>C	V582L
IGHM	X17115	147020	GEN-1ZX	Human mRNA for IgM heavy chain complete sequence	2006	1934T>A	3
HLA-G	X17273	142871	GEN-205	Human HLA G (HLA 6.0) mRNA for non classical class I transplantation antigen	20	15G>A	S
HLA-G	X17273	142871	GEN-205	Human HLA G (HLA 6.0) mRNA for non classical class I transplantation antigen	41	36G>A	S

HLA-G	X17273	142871	GEN-205	Human HLA G (HLA 6.0) mRNA for non classical class I transplantation antigen	248	243G>A	S
HLA-G	X17273	142871	GEN-205	Human HLA G (HLA 6.0) mRNA for non classical class I transplantation antigen	356	351C>T	S
HLA-G	X17273	142871	GEN-205	Human HLA G (HLA 6.0) mRNA for non classical class I transplantation antigen	812	807A>C	S
HLA-G	X17273	142871	GEN-205	Human HLA G (HLA 6.0) mRNA for non classical class I transplantation antigen	839	834G>A	S
HLA-G	X17273	142871	GEN-205	Human HLA G (HLA 6.0) mRNA for non classical class I transplantation antigen	947	942C>T	S
HLA-G	X17273	142871	GEN-205	Human HLA G (HLA 6.0) mRNA for non classical class I transplantation antigen	1004	999A>G	S
HLA-G	X17273	142871	GEN-205	Human HLA G (HLA 6.0) mRNA for non classical class I transplantation antigen	1123	1118G>C	3
HLA-G	X17273	142871	GEN-205	Human HLA G (HLA 6.0) mRNA for non classical class I transplantation antigen	1140	1135C>A	3
HLA-G	X17273	142871	GEN-205	Human HLA G (HLA 6.0) mRNA for non classical class I transplantation antigen	1148	1143C>T	3
HLA-G	X17273	142871	GEN-205	Human HLA G (HLA 6.0) mRNA for non classical class I transplantation antigen	1254	1249T>G	3
HLA-G	X17273	142871	GEN-205	Human HLA G (HLA 6.0) mRNA for non classical class I transplantation antigen	1255	1250C>G	3

mRNA for non classical class I transplantation antigen									
X51362	X51362	126450	GEN-31W	Dopamine Receptor D2	588	423G>A	S		
X51362	X51362	126450	GEN-31W	Dopamine Receptor D2	1104	939C>T	S		
X51362	X51362	126450	GEN-31W	Dopamine Receptor D2	1122	957T>C	S		
X51362	X51362	126450	GEN-31W	Dopamine Receptor D2	1248	1083A>G	S		
X51362	X51362	126450	GEN-31W	Dopamine Receptor D2	1488	1323T>C	S		
X51362	X51362	126450	GEN-31W	Dopamine Receptor D2	1548	1383A>G	3		
X51362	X51362	126450	GEN-31W	Dopamine Receptor D2	2361	2196C>T	3		
EDN3	X52001	131242	GEN-33E	Endothelin 3	1262	1152G>A	3		
EDN3	X52001	131242	GEN-33E	Endothelin 3	1649	1539C>G	3		
EDN3	X52001	131242	GEN-33E	Endothelin 3	1700	1590C>T	3		
EDN3	X52001	131242	GEN-33E	Endothelin 3	1742	1632C>T	3		
EDN3	X52001	131242	GEN-33E	Endothelin 3	1797	1687C>T	3		
EDN3	X52001	131242	GEN-33E	Endothelin 3	1914	1804G>C	3		
EDN3	X52001	131242	GEN-33E	Endothelin 3	2040	1930C>T	3		
X52079	X52079	602272	GEN-33B	H.sapiens transcription factor (ITF-2) mRNA, 3 end	979	979T>G	S327A		
X52079	X52079	602272	GEN-33B	H.sapiens transcription factor (ITF-2) mRNA, 3 end	1794	1794G>A	S		
X52425	X52425	147781	GEN-59	Interleukin 4 receptor	3044	2869G>A	3		
X52425	X52425	147781	GEN-59	Interleukin 4 receptor	3289	3114A>G	3		
X52425	X52425	147781	GEN-59	Interleukin 4 receptor	3391	3216C>T	3		
X52479	X52479	176960	GEN-LM	Protein kinase C, alpha	908	881A>C	D294A		
CD22	X52785	107266	GEN-33Z	H.sapiens CD22 mRNA	1357	1323C>T	S		

CD22	X52785	107266	GEN-33Z	H.sapiens CD22 mRNA	1531	1497C>T	S
CHRNA3	X53559	118503	GEN-34I	Nicotinic, Cholinergic receptor alpha 3	212	212A>G	D71G
CHRNA3	X53559	118503	GEN-34I	Nicotinic, Cholinergic receptor alpha 3	552	552C>T	S
KAI1	X53795	600623	GEN-34P	Human R2 mRNA for an inducible membrane protein	510	354C>T	S
KAI1	X53795	600623	GEN-34P	Human R2 mRNA for an inducible membrane protein	1196	1040G>T	3
KAI1	X53795	600623	GEN-34P	Human R2 mRNA for an inducible membrane protein	1309	1153G>A	3
KAI1	X53795	600623	GEN-34P	Human R2 mRNA for an inducible membrane protein	1325	1169G>A	3
KAI1	X53795	600623	GEN-34P	Human R2 mRNA for an inducible membrane protein	1335	1179G>A	3
KAI1	X53795	600623	GEN-34P	Human R2 mRNA for an inducible membrane protein	1362	1206C>T	3
KAI1	X53795	600623	GEN-34P	Human R2 mRNA for an inducible membrane protein	1367	1211C>T	3
KAI1	X53795	600623	GEN-34P	Human R2 mRNA for an inducible membrane protein	1368	1212G>A	3
KAI1	X53795	600623	GEN-34P	Human R2 mRNA for an inducible membrane protein	1370	1214G>A	3
KAI1	X53795	600623	GEN-34P	Human R2 mRNA for an inducible membrane protein	1371	1215T>C	3
KAI1	X53795	600623	GEN-34P	Human R2 mRNA for an inducible membrane protein	1378	1222C>T	3
KAI1	X53795	600623	GEN-34P	Human R2 mRNA for an inducible membrane protein	1382	1226G>A	3

KAI1	X53795	600623	GEN-34P	Human R2 mRNA for an inducible membrane protein	1392	1236C>T	3
KAI1	X53795	600623	GEN-34P	Human R2 mRNA for an inducible membrane protein	1423	1267C>T	3
X54101	X54101	None	GEN-34W	Human NKG5 mRNA, expressed in natural killer cells and T-cells	484	356C>T	T119I
X54101	X54101	None	GEN-34W	Human NKG5 mRNA, expressed in natural killer cells and T-cells	625	497C>G	3
X54101	X54101	None	GEN-34W	Human NKG5 mRNA, expressed in natural killer cells and T-cells	717	589C>G	3
FCAR	X54150	147045	GEN-34T	Human mRNA for Fc receptor	363	324A>G	S
X54199	X54199	138440	GEN-LS	Phosphoribosylglycinamide formyltransferase, phosphoribosylglycinamide synthetase, phosphoribosylaminoimidazole synthetase	168	90G>A	S
X54315	X54315	114020	GEN-351	Human mRNA for N-cadherin	2549	2448T>C	S
X54867	X54867	161555	GEN-MIV	Human mRNA for NKG2-A gene	1188	1024G>C	3
X54867	X54867	161555	GEN-MIV	Human mRNA for NKG2-A gene	1214	1050T>A	3
X54867	X54867	161555	GEN-MIV	Human mRNA for NKG2-A gene	1232	1068A>T	3
X54867	X54867	161555	GEN-MIV	Human mRNA for NKG2-A gene	1269	1105G>A	3
X54867	X54867	161555	GEN-MIV	Human mRNA for NKG2-A gene	1353	1189C>T	3
X55415	X55415	137060	GEN-364	Human mRNA for UDP_galactose:N-acetylglucosaminide-(beta 1->4) galactosyltransferase	28	(-12)G>C	5

X55415	X55415	137060	GEN-364	Human mRNA for UDP_galactose:N- acetylglucosaminide-(beta 1->4)	30	(-10)C>G	5
X55415	X55415	137060	GEN-364	galactosyltransferase Human mRNA for UDP_galactose:N- acetylglucosaminide-(beta 1->4)	531	492G>A	S
X55415	X55415	137060	GEN-364	galactosyltransferase Human mRNA for UDP_galactose:N- acetylglucosaminide-(beta 1->4)	770	731A>G	H244R
X55415	X55415	137060	GEN-364	galactosyltransferase Human mRNA for UDP_galactose:N- acetylglucosaminide-(beta 1->4)	1041	1002G>A	S
X55740	X55740	129190	GEN-36H	galactosyltransferase Human placental cDNA coding for 5nucleotidase (EC 3.1.3.5)	3373	3324T>G	3
CRP	X56692	123260	GEN-373	H.sapiens mRNA for C- reactive protein	330	241A>G	I81V
CRP	X56692	123260	GEN-373	H.sapiens mRNA for C- reactive protein	636	547G>A	V183M
CRP	X56692	123260	GEN-373	H.sapiens mRNA for C- reactive protein	1020	931G>A	3
YWHAB	X57346	601289	GEN-37R	H.sapiens mRNA for HS1 protein	432	60C>A	S
YWHAB	X57346	601289	GEN-37R	H.sapiens mRNA for HS1 protein	1135	763T>C	3
X57348	X57348	601290	GEN-37S	H.sapiens mRNA (clone 9112)	1317	1152C>T	3
X57348	X57348	601290	GEN-37S	H.sapiens mRNA (clone 9112)	1342	1177C>T	3
X57522	X57522	170260	GEN-37W	H.sapiens RING4 cDNA	1207	1177A>G	I393V
X57522	X57522	170260	GEN-37W	H.sapiens RING4 cDNA	2120	2090A>G	D697G

X57819	X57819	None	GEN-389	Human rearranged immunoglobulin lambda light chain mRNA	499	499T>C	C167R
X57819	X57819	None	GEN-389	Human rearranged immunoglobulin lambda light chain mRNA	524	524G>A	F
X57819	X57819	None	GEN-389	Human rearranged immunoglobulin lambda light chain mRNA	545	545G>A	S182N
X57819	X57819	None	GEN-389	Human rearranged immunoglobulin lambda light chain mRNA	558	558A>C	Q186H
X57819	X57819	None	GEN-389	Human rearranged immunoglobulin lambda light chain mRNA	571	571G>A	E191K
X57819	X57819	None	GEN-389	Human rearranged immunoglobulin lambda light chain mRNA	616	616C>T	F
X57819	X57819	None	GEN-389	Human rearranged immunoglobulin lambda light chain mRNA	639	639G>A	S
X57819	X57819	None	GEN-389	Human rearranged immunoglobulin lambda light chain mRNA	695	695A>G	Y232C
X57819	X57819	None	GEN-389	Human rearranged immunoglobulin lambda light chain mRNA	714	714C>T	3
X57819	X57819	None	GEN-389	Human rearranged immunoglobulin lambda light chain mRNA	724	724C>T	3
X57830	X57830	182135	GEN-7V	Serotonin 5-HT2 receptor	247	102T>C	S
X58377	X58377	147681	GEN-38V	Interleukin 11	807	744A>G	3
X58377	X58377	147681	GEN-38V	Interleukin 11	927	864T>G	3
X58377	X58377	147681	GEN-38V	Interleukin 11	1964	1901T>C	3
BTK	X58957	300300	GEN-39A	H.sapiens atk mRNA for agammaglobulinaemia tyrosine kinase	2228	2096A>C	3
BTK	X58957	300300	GEN-	H.sapiens atk mRNA for	2304	2172A>G	3

SD-144146.1

X60069	X60069	231950	GEN-3AJ	glutamyltransferase Human mRNA for pancreatic gamma-glutamyltransferase	1624	1266C>T	S
X60069	X60069	231950	GEN-3AJ	glutamyltransferase Human mRNA for pancreatic gamma-glutamyltransferase	1637	1279C>A	P427T
X60069	X60069	231950	GEN-3AJ	glutamyltransferase Human mRNA for pancreatic gamma-glutamyltransferase	1651	1293C>T	S
X60069	X60069	231950	GEN-3AJ	glutamyltransferase Human mRNA for pancreatic gamma-glutamyltransferase	1662	1304T>C	V435A
X60069	X60069	231950	GEN-3AJ	glutamyltransferase Human mRNA for pancreatic gamma-glutamyltransferase	1783	1425A>G	S
X60069	X60069	231950	GEN-3AJ	glutamyltransferase Human mRNA for pancreatic gamma-glutamyltransferase	1794	1436C>T	T479M
X60069	X60069	231950	GEN-3AJ	glutamyltransferase Human mRNA for pancreatic gamma-glutamyltransferase	1795	1437G>A	S
X60069	X60069	231950	GEN-3AJ	glutamyltransferase Human mRNA for pancreatic gamma-glutamyltransferase	1981	1623C>T	S
X60069	X60069	231950	GEN-3AJ	glutamyltransferase Human mRNA for pancreatic gamma-glutamyltransferase	2007	1649C>T	T550M
X60069	X60069	231950	GEN-3AJ	glutamyltransferase Human mRNA for pancreatic gamma-glutamyltransferase	2031	1673C>T	S558L
X60069	X60069	231950	GEN-3AJ	glutamyltransferase Human mRNA for pancreatic gamma-glutamyltransferase	2047	1689C>T	S
X60069	X60069	231950	GEN-3AJ	glutamyltransferase Human mRNA for pancreatic gamma-glutamyltransferase	2147	1789C>T	3
X60069	X60069	231950	GEN-3AJ	glutamyltransferase Human mRNA for pancreatic gamma-glutamyltransferase	2176	1818C>T	3
X60069	X60069	231950	GEN-3AJ	glutamyltransferase Human mRNA for pancreatic gamma-glutamyltransferase	2224	1866C>A	3

X60992	X60992	186720	GEN-3B1	3AJ	pancreatic gamma-glutamyltransferase	2556	2436T>C	3
X61157	X61157	109635	GEN-23		H.sapiens CD6 mRNA for T cell glycoprotein CD6	203	96A>C	S
X61157	X61157	109635	GEN-23		Adrenergic receptor (Beta kinase 1-phosphorylates beta adrenergic receptor)	1372	1265A>G	H422R
X61157	X61157	109635	GEN-23		Adrenergic receptor (Beta kinase 1-phosphorylates beta adrenergic receptor)	1501	1394G>A	R465K
X61157	X61157	109635	GEN-23		Adrenergic receptor (Beta kinase 1-phosphorylates beta adrenergic receptor)	1766	1659C>T	S
X61157	X61157	109635	GEN-23		Adrenergic receptor (Beta kinase 1-phosphorylates beta adrenergic receptor)	1823	1716T>C	S
X61157	X61157	109635	GEN-23		Adrenergic receptor (Beta kinase 1-phosphorylates beta adrenergic receptor)	2976	2869G>A	3
NFKB2	X61498	164012	GEN-3BW		Adrenergic receptor (Beta kinase 1-phosphorylates beta adrenergic receptor)	2457	2294C>T	P765L
KDR	X61656	191306	GEN-3BZ		H.sapiens mRNA for NF-kB subunit	2308	2308A>G	T770A
KDR	X61656	191306	GEN-3BZ		H.sapiens mRNA for growth factor receptor tyrosine kinase	2353	2353G>C	G785R
KDR	X61656	191306	GEN-3BZ		H.sapiens mRNA for growth factor receptor tyrosine kinase	2499	2499C>G	N833K
KDR	X61656	191306	GEN-3BZ		H.sapiens mRNA for growth factor receptor tyrosine kinase	2537	2537A>T	E846V
KDR	X61656	191306	GEN-3BZ		H.sapiens mRNA for growth factor receptor tyrosine kinase	4123	4123G>C	3
X62572	X62572	146790	GEN-3CL		H.sapiens RNA for Fc receptor, PC23	967	968T>C	3

X62572	X62572	146790	GEN-3CL	H.sapiens RNA for Fc receptor, PC23	1240	1241A>G	3
X62572	X62572	146790	GEN-3CL	H.sapiens RNA for Fc receptor, PC23	1300	1301C>T	3
X62572	X62572	146790	GEN-3CL	H.sapiens RNA for Fc receptor, PC23	1542	1543G>C	3
X62572	X62572	146790	GEN-3CL	H.sapiens RNA for Fc receptor, PC23	1560	1561C>A	3
X62572	X62572	146790	GEN-3CL	H.sapiens RNA for Fc receptor, PC23	1709	1710T>G	3
X62572	X62572	146790	GEN-3CL	H.sapiens RNA for Fc receptor, PC23	1931	1932A>T	3
X62572	X62572	146790	GEN-3CL	H.sapiens RNA for Fc receptor, PC23	2032	2033G>A	3
X62572	X62572	146790	GEN-3CL	H.sapiens RNA for Fc receptor, PC23	2136	2137G>A	3
X62572	X62572	146790	GEN-3CL	H.sapiens RNA for Fc receptor, PC23	2176	2177C>T	3
X62572	X62572	146790	GEN-3CL	H.sapiens RNA for Fc receptor, PC23	2201	2202G>A	3
X62744	X62744	142855	GEN-3CQ	Human RING6 mRNA for HLA class II alpha chain-like product	541	496G>A	V166I
X62744	X62744	142855	GEN-3CQ	Human RING6 mRNA for HLA class II alpha chain-like product	674	629G>A	R210H
X62744	X62744	142855	GEN-3CQ	Human RING6 mRNA for HLA class II alpha chain-like product	750	705G>C	S
X62744	X62744	142855	GEN-3CQ	Human RING6 mRNA for HLA class II alpha chain-like product	1081	1036A>T	3
X63053	X63053	602492	GEN-3D4	H.sapiens PTX3 mRNA	1689	1684G>A	3
TCRB	X63456	186930	GEN-3DG	H.sapiens mRNA for T-cell antigen receptor beta-chain	421	411G>C	K137N
TCRB	X63456	186930	GEN-3DG	H.sapiens mRNA for T-cell antigen receptor beta-chain	496	486G>A	S
TCRB	X63456	186930	GEN-	H.sapiens mRNA for T-cell	516	506T>A	F169Y

TCRB	X63456	186930	3DG	antigen receptor beta-chain	520	510C>T	S
			GEN-3DG	H.sapiens mRNA for T-cell antigen receptor beta-chain			
TCRB	X63456	186930	3DG	antigen receptor beta-chain	580	570A>G	S
			GEN-3DG	H.sapiens mRNA for T-cell antigen receptor beta-chain			
TCRB	X63456	186930	3DG	antigen receptor beta-chain	754	744C>T	S
			GEN-3DG	H.sapiens mRNA for T-cell antigen receptor beta-chain			
TCRB	X63456	186930	3DG	antigen receptor beta-chain	805	795T>C	S
			GEN-3DG	H.sapiens mRNA for T-cell antigen receptor beta-chain			
TCRB	X63456	186930	3DG	antigen receptor beta-chain	811	801G>C	S
			GEN-3DG	H.sapiens mRNA for T-cell antigen receptor beta-chain			
TCRB	X63456	186930	3DG	antigen receptor beta-chain	813	803T>A	V268E
			GEN-3DG	H.sapiens mRNA for T-cell antigen receptor beta-chain			
TCRB	X63456	186930	3DG	antigen receptor beta-chain	817	807C>T	S
			GEN-3DG	H.sapiens mRNA for T-cell antigen receptor beta-chain			
TCRB	X63456	186930	3DG	antigen receptor beta-chain	860	850C>T	S
			GEN-3DG	H.sapiens mRNA for T-cell antigen receptor beta-chain			
TCRB	X63456	186930	3DG	antigen receptor beta-chain	878	868C>A	L290M
			GEN-3DG	H.sapiens mRNA for T-cell antigen receptor beta-chain			
X65019	X65019	147678	GEN-6G	INTERLEUKIN 1 BETA CONVERTASE PRECURSOR	51	44G>A	R15H
X65019	X65019	147678	GEN-6G	INTERLEUKIN 1 BETA CONVERTASE PRECURSOR	116	109A>C	K37Q
X65019	X65019	147678	GEN-6G	INTERLEUKIN 1 BETA CONVERTASE PRECURSOR	261	254G>A	G85E
X66403	X66403	100725	GEN-5D	Nicotinic, Cholinergic receptor epsilon polypeptide	2236	2225G>T	3

X66403	X66403	100725	GEN-5D	Nicotinic, Cholinergic receptor epsilon	2333	2322A>G	3
X66403	X66403	100725	GEN-5D	Nicotinic, Cholinergic receptor epsilon	2364	2353G>T	3
CD44	X66733	107269	GEN-3H2	H.sapiens mRNA for epican	384	255C>T	S
CD44	X66733	107269	GEN-3H2	H.sapiens mRNA for epican	455	326C>A	S109Y
X67325	X67325	600009	GEN-25	Interferon alpha inducible protein 27	311	257G>A	S86N
X67325	X67325	600009	GEN-25	Interferon alpha inducible protein 27	320	266G>C	G89A
X67325	X67325	600009	GEN-25	Interferon alpha inducible protein 27	485	431C>G	3
X67699	X67699	114280	GEN-3HP	H.sapiens HE5 mRNA for CDw52 antigen	143	119G>A	S40N
X67699	X67699	114280	GEN-3HP	H.sapiens HE5 mRNA for CDw52 antigen	147	123G>A	M41I
X68596	X68596	168468	GEN-3IJ	H.sapiens mRNA for parathyroid hormone receptor	1563	1389T>C	S
X69117	X69117	109636	GEN-5G	BETA-ADRENERGIC RECEPTOR KINASE 2	1182	1182T>C	S
X69117	X69117	109636	GEN-5G	BETA-ADRENERGIC RECEPTOR KINASE 2	1609	1609G>A	E537K
X69819	X69819	146631	GEN-28	Intercellular adhesion molecule 3	195	187A>G	I63V
X69819	X69819	146631	GEN-28	Intercellular adhesion molecule 3	317	309C>T	S
X69819	X69819	146631	GEN-28	Intercellular adhesion molecule 3	436	428G>A	G143D
X69819	X69819	146631	GEN-28	Intercellular adhesion molecule 3	1172	1164G>A	S
X69819	X69819	146631	GEN-28	Intercellular adhesion molecule 3	1219	1211G>A	R404Q
X70340	X70340	190170	GEN-S3	H.sapiens mRNA for transforming growth factor alpha	3756	3725C>G	3
X70811	X70811	109691	GEN-	beta-3-adrenergic receptor	315	190T>C	W64R

X70811	X70811	109691	3KK GEN-	beta-3-adrenergic receptor	315	190T>C	W64R
ENG	X72012	131195	3KK GEN-3L3	H.sapiens end mRNA for endoglin	1165	884C>G	T295R
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	1380	1155C>T	S
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	1503	1278C>T	S
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	2048	1823C>T	S608L
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	2287	2062G>A	G688S
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	2339	2114A>G	D705G
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	2583	2358T>C	S
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	2982	2757A>G	S
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	3022	2797C>G	R933G
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	3051	2826C>T	S
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	3693	3468T>C	3
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	3715	3490G>A	3
RGS1	X73427	600323	GEN-3M6	H.sapiens 1:20 mRNA for alpha helical basic phosphoprotein	247	233C>T	A78V
MHC2TA	X74301	600005	GEN-3N5	H.sapiens mRNA for MHC class II transactivator	1614	1499C>G	A500G
MHC2TA	X74301	600005	GEN-3N5	H.sapiens mRNA for MHC class II transactivator	3759	3644G>A	3
MHC2TA	X74301	600005	GEN-3N5	H.sapiens mRNA for MHC class II transactivator	4422	4307T>C	3
X75913	X75913	601269	GEN-3OG	H.sapiens mRNA for gC1q-R	1052	974A>G	3
X75913	X75913	601269	GEN-3OG	H.sapiens mRNA for gC1q-R	1074	996T>C	3
X75962	X75962	600315	GEN-	H.sapiens mRNA for OX40	836	831C>T	S

SD-144146.1

LIPA	X76488	278000	MNA GEN-3P2	homologue H.sapiens mRNA for lysosomal acid lipase	191	46A>C	T16P
LIPA	X76488	278000	GEN-3P2	H.sapiens mRNA for lysosomal acid lipase	212	67G>A	G23R
LIPA	X76488	278000	GEN-3P2	H.sapiens mRNA for lysosomal acid lipase	967	822G>A	M274I
LIPA	X76488	278000	GEN-3P2	H.sapiens mRNA for lysosomal acid lipase	1531	1386C>T	3
LIPA	X76488	278000	GEN-3P2	H.sapiens mRNA for lysosomal acid lipase	2254	2109A>T	3
LIPA	X76488	278000	GEN-3P2	H.sapiens mRNA for lysosomal acid lipase	2439	2294C>T	3
X77130	X77130	602548	GEN-4FN	H.sapiens mRNA for ORL1 receptor	528	351G>A	S
X77130	X77130	602548	GEN-4FN	H.sapiens mRNA for ORL1 receptor	569	392A>G	Y131C
X77130	X77130	602548	GEN-4FN	H.sapiens mRNA for ORL1 receptor	687	510C>T	S
X77130	X77130	602548	GEN-4FN	H.sapiens mRNA for ORL1 receptor	1303	1126C>G	3
X77130	X77130	602548	GEN-4FN	H.sapiens mRNA for ORL1 receptor	1601	1424T>G	3
X77130	X77130	602548	GEN-4FN	H.sapiens mRNA for ORL1 receptor	1816	1639G>T	3
X77722	X77722	602376	GEN-29	Interferon (alpha,beta, omega) receptor 2 (splice variant)	253	28G>T	V10F
X77722	X77722	602376	GEN-29	Interferon (alpha,beta, omega) receptor 2 (splice variant)	1128	903A>G	S
ID1	X77956	600349	GEN-3QL	H.sapiens Id1 mRNA	380	345G>A	S
ID1	X77956	600349	GEN-3QL	H.sapiens Id1 mRNA	382	347C>A	T116N
ID1	X77956	600349	GEN-3QL	H.sapiens Id1 mRNA	842	807A>C	3
ID1	X77956	600349	GEN-3QL	H.sapiens Id1 mRNA	851	816G>A	3
YWHAH	X78138	113508	GEN-3QU	H.sapiens 14-3-3 eta subtype mRNA	953	753A>G	3

YWHAH	X78138	113508	GEN-3QU	H.sapiens 14-3-3 eta subtype mRNA	960	760G>A	3
YWHAH	X78138	113508	GEN-3QU	H.sapiens 14-3-3 eta subtype mRNA	1387	1187C>T	3
X78282	X78282	601292	GEN-LVF	H.sapiens mRNA for aryl sulfotransferase (ST1A2)	895	895T>C	3
X78706	X78706	600184	GEN-2A	Carnitine Acetyltransferase	1922	1922G>A	3
X78706	X78706	600184	GEN-2A	Carnitine Acetyltransferase	2378	2378G>A	3
X78706	X78706	600184	GEN-2A	Carnitine Acetyltransferase	2382	2382G>A	3
X79483	X79483	602399	GEN-LPR	H.sapiens ERK6 mRNA for extracellular signal regulated kinase	1287	1254T>G	3
X80200	X80200	None	GEN-3UL	H.sapiens MLN62 mRNA	1581	1496C>A	3
X80200	X80200	None	GEN-3UL	H.sapiens MLN62 mRNA	1684	1599G>A	3
IGHG3	X81695	147120	GEN-3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3 region	528	529C>T	3
IGHG3	X81695	147120	GEN-3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3 region	534	535C>T	3
IGHG3	X81695	147120	GEN-3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3 region	594	595T>C	3
IGHG3	X81695	147120	GEN-3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3 region	601	602A>C	3
IGHG3	X81695	147120	GEN-3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3 region	668	669A>T	3
IGHG3	X81695	147120	GEN-3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3 region	726	727T>C	3
IGHG3	X81695	147120	GEN-3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3 region	796	797G>A	3
IGHG3	X81695	147120	GEN-3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3 region	804	805G>A	3
IGHG3	X81695	147120	GEN-3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3 region	827	828A>T	3

IGHG3	X81695	147120	3W4	VH-D-JH-Hinge-CH2-CH3 region	828	829C>T	3
IGHG3	X81695	147120	GEN- 3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3	842	843C>T	3
IGHG3	X81695	147120	GEN- 3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3	849	850G>T	3
IGHG3	X81695	147120	GEN- 3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3	853	854A>C	3
IGHG3	X81695	147120	GEN- 3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3	900	901T>C	3
IGHG3	X81695	147120	GEN- 3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3	905	906G>A	3
IGHG3	X81695	147120	GEN- 3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3	916	917G>A	3
IGHG3	X81695	147120	GEN- 3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3	957	958G>C	3
IGHG3	X81695	147120	GEN- 3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3	963	964G>A	3
IGHG3	X81695	147120	GEN- 3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3	970	971G>A	3
IGHG3	X81695	147120	GEN- 3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3	973	974C>G	3
IGHG3	X81695	147120	GEN- 3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3	999	1000C>T	3
IGHG3	X81695	147120	GEN- 3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3	1002	1003T>C	3

IGHG3	X81695	147120	GEN-3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3 region	1012	1013A>C	3
IGHG3	X81695	147120	GEN-3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3 region	1045	1046G>A	3
IGHG3	X81695	147120	GEN-3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3 region	1050	1051C>T	3
IGHG3	X81695	147120	GEN-3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3 region	1073	1074C>G	3
IGHG3	X81695	147120	GEN-3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3 region	1075	1076C>T	3
IGHG3	X81695	147120	GEN-3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3 region	1088	1089A>T	3
IGHG3	X81695	147120	GEN-3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3 region	1092	1093G>A	3
IGHG3	X81695	147120	GEN-3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3 region	1113	1114C>T	3
IGHG3	X81695	147120	GEN-3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3 region	1130	1131G>C	3
IGHG3	X81695	147120	GEN-3W4	H.sapiens rearranged IgG VH-D-JH-Hinge-CH2-CH3 region	1137	1138G>A	3
X82321	X82321	None	GEN-3WT	H.sapiens mRNA for thiol-specific antioxidant	304	304G>A	G102R
X82321	X82321	None	GEN-3WT	H.sapiens mRNA for thiol-specific antioxidant	422	422G>T	W141L
X82321	X82321	None	GEN-3WT	H.sapiens mRNA for thiol-specific antioxidant	640	640C>G	3
X82321	X82321	None	GEN-3WT	H.sapiens mRNA for thiol-specific antioxidant	655	655C>T	3
HLA-C	X83394	142840	GEN-3XX	H.sapiens mRNA for HLA-Cw*0704	43	22G>A	A8T
HLA-C	X83394	142840	GEN-	H.sapiens mRNA for HLA-	49	28C>A	L10I

HLA-C	X83394	142840	3XX GEN- 3XX	Cw*0704 H.sapiens mRNA for HLA- Cw*0704	68	47G>C	G16A
HLA-C	X83394	142840	3XX GEN- 3XX	H.sapiens mRNA for HLA- Cw*0704	80	59C>T	T20I
HLA-C	X83394	142840	3XX GEN- 3XX	H.sapiens mRNA for HLA- Cw*0704	94	73T>G	C25G
HLA-C	X83394	142840	3XX GEN- 3XX	H.sapiens mRNA for HLA- Cw*0704	118	97G>T	D33Y
HLA-C	X83394	142840	3XX GEN- 3XX	H.sapiens mRNA for HLA- Cw*0704	126	105C>T	S
HLA-C	X83394	142840	3XX GEN- 3XX	H.sapiens mRNA for HLA- Cw*0704	155	134G>A	R45H
HLA-C	X83394	142840	3XX GEN- 3XX	H.sapiens mRNA for HLA- Cw*0704	163	142T>G	S48A
HLA-C	X83394	142840	3XX GEN- 3XX	H.sapiens mRNA for HLA- Cw*0704	222	201G>A	S
HLA-C	X83394	142840	3XX GEN- 3XX	H.sapiens mRNA for HLA- Cw*0704	234	213C>G	S
HLA-C	X83394	142840	3XX GEN- 3XX	H.sapiens mRNA for HLA- Cw*0704	239	218C>A	A73E
HLA-C	X83394	142840	3XX GEN- 3XX	H.sapiens mRNA for HLA- Cw*0704	291	270G>C	K90N
HLA-C	X83394	142840	3XX GEN- 3XX	H.sapiens mRNA for HLA- Cw*0704	310	289G>A	A97T
HLA-C	X83394	142840	3XX GEN- 3XX	H.sapiens mRNA for HLA- Cw*0704	323	302G>A	S101N
HLA-C	X83394	142840	3XX GEN- 3XX	H.sapiens mRNA for HLA- Cw*0704	333	312C>A	N104K
HLA-C	X83394	142840	3XX GEN- 3XX	H.sapiens mRNA for HLA- Cw*0704	362	341A>C	D114A
HLA-C	X83394	142840	3XX GEN- 3XX	H.sapiens mRNA for HLA- Cw*0704	374	353C>T	T118I
HLA-C	X83394	142840	3XX GEN- 3XX	H.sapiens mRNA for HLA- Cw*0704	382	361A>T	R121W
HLA-C	X83394	142840	3XX GEN- 3XX	H.sapiens mRNA for HLA- Cw*0704	408	387C>G	S
HLA-C	X83394	142840	3XX GEN- 3XX	H.sapiens mRNA for HLA- Cw*0704	430	409T>C	Y137H
HLA-C	X83394	142840	3XX GEN- 3XX	H.sapiens mRNA for HLA- Cw*0704	433	412G>A	D138N

HLA-C	X83394	142840	GEN- 3XX	H.sapiens mRNA for HLA-Cw*0704	441	420C>A	F140L
HLA-C	X83394	142840	GEN- 3XX	H.sapiens mRNA for HLA-Cw*0704	474	453C>T	S
HLA-C	X83394	142840	GEN- 3XX	H.sapiens mRNA for HLA-Cw*0704	480	459C>T	S
HLA-C	X83394	142840	GEN- 3XX	H.sapiens mRNA for HLA-Cw*0704	495	474C>T	S
HLA-C	X83394	142840	GEN- 3XX	H.sapiens mRNA for HLA-Cw*0704	507	486C>G	S
HLA-C	X83394	142840	GEN- 3XX	H.sapiens mRNA for HLA-Cw*0704	520	499A>T	T167S
HLA-C	X83394	142840	GEN- 3XX	H.sapiens mRNA for HLA-Cw*0704	533	512T>G	L171W
HLA-C	X83394	142840	GEN- 3XX	H.sapiens mRNA for HLA-Cw*0704	548	527C>A	A176E
HLA-C	X83394	142840	GEN- 3XX	H.sapiens mRNA for HLA-Cw*0704	622	601A>G	K201E
HLA-C	X83394	142840	GEN- 3XX	H.sapiens mRNA for HLA-Cw*0704	626	605C>A	T202K
HLA-C	X83394	142840	GEN- 3XX	H.sapiens mRNA for HLA-Cw*0704	639	618G>A	S
HLA-C	X83394	142840	GEN- 3XX	H.sapiens mRNA for HLA-Cw*0704	644	623C>A	P208H
HLA-C	X83394	142840	GEN- 3XX	H.sapiens mRNA for HLA-Cw*0704	669	648C>T	S
HLA-C	X83394	142840	GEN- 3XX	H.sapiens mRNA for HLA-Cw*0704	673	652C>G	L218V
HLA-C	X83394	142840	GEN- 3XX	H.sapiens mRNA for HLA-Cw*0704	724	703G>A	A235T
HLA-C	X83394	142840	GEN- 3XX	H.sapiens mRNA for HLA-Cw*0704	748	727C>T	R243W
HLA-C	X83394	142840	GEN- 3XX	H.sapiens mRNA for HLA-Cw*0704	756	735G>C	S
HLA-C	X83394	142840	GEN- 3XX	H.sapiens mRNA for HLA-Cw*0704	765	744G>A	S
HLA-C	X83394	142840	GEN- 3XX	H.sapiens mRNA for HLA-Cw*0704	768	747C>T	S
HLA-C	X83394	142840	GEN- 3XX	H.sapiens mRNA for HLA-Cw*0704	777	756C>T	S
HLA-C	X83394	142840	GEN- 3XX	H.sapiens mRNA for HLA-Cw*0704	835	814G>A	V272M

HLA-C	X83394	142840	3XX	GEN-3XX	Cw*0704 H.sapiens mRNA for HLA-Cw*0704	850	829C>G	Q277E
HLA-C	X83394	142840	3XX	GEN-3XX	H.sapiens mRNA for HLA-Cw*0704	874	853A>G	M285V
HLA-C	X83394	142840	3XX	GEN-3XX	H.sapiens mRNA for HLA-Cw*0704	893	872A>C	Q291P
HLA-C	X83394	142840	3XX	GEN-3XX	H.sapiens mRNA for HLA-Cw*0704	912	891C>A	S297R
HLA-C	X83394	142840	3XX	GEN-3XX	H.sapiens mRNA for HLA-Cw*0704	933	912C>T	S
HLA-C	X83394	142840	3XX	GEN-3XX	H.sapiens mRNA for HLA-Cw*0704	946	925A>G	M309V
HLA-C	X83394	142840	3XX	GEN-3XX	H.sapiens mRNA for HLA-Cw*0704	977	956T>C	V319A
HLA-C	X83394	142840	3XX	GEN-3XX	H.sapiens mRNA for HLA-Cw*0704	1012	991A>G	M331V
HLA-C	X83394	142840	3XX	GEN-3XX	H.sapiens mRNA for HLA-Cw*0704	1070	1049G>C	C350S
HLA-C	X83394	142840	3XX	GEN-3XX	H.sapiens mRNA for HLA-Cw*0704	1108	1087A>G	T363A
X83861	X83861	176806	3XX	GEN-5H	Prostaglandin E receptor 3 (subtype EP3) {alternative products}	387	180C>G	S
X84213	X84213	600516	GEN-3ZC	GEN-3ZC	H.sapiens BAK mRNA for BCI-2 homologue	32	(-161)C>T	5
X84213	X84213	600516	GEN-3ZC	GEN-3ZC	H.sapiens BAK mRNA for BCI-2 homologue	317	125G>A	R42H
X84213	X84213	600516	GEN-3ZC	GEN-3ZC	H.sapiens BAK mRNA for BCI-2 homologue	435	243C>T	S
X84213	X84213	600516	GEN-3ZC	GEN-3ZC	H.sapiens BAK mRNA for BCI-2 homologue	616	424G>A	V142I
X84213	X84213	600516	GEN-3ZC	GEN-3ZC	H.sapiens BAK mRNA for BCI-2 homologue	663	471C>T	S
X84213	X84213	600516	GEN-3ZC	GEN-3ZC	H.sapiens BAK mRNA for BCI-2 homologue	900	708T>C	3
X84213	X84213	600516	GEN-3ZC	GEN-3ZC	H.sapiens BAK mRNA for BCI-2 homologue	974	782C>T	3
CD97	X84700	601211	GEN-3ZO	GEN-3ZO	H.sapiens mRNA for leucocyte antigen CD97	828	758C>G	P253R
X86474	X86474	600250	GEN-3ZO	GEN-3ZO	H.sapiens mRNA for ATAC	249	225A>G	S

X86474	X86474	600250	40W GEN-	H.sapiens mRNA for ATAC protein	357	333T>C	S
X86474	X86474	600250	40W GEN-	H.sapiens mRNA for ATAC protein	423	399G>C	3
X86474	X86474	600250	40W GEN-	H.sapiens mRNA for ATAC protein	446	422G>A	3
X86681	X86681	602110	40W GEN-	H.sapiens mRNA for ATAC protein	1725	1340G>A	3
X97058	X97058	602451	41E GEN-	H.sapiens mRNA for nucleolar protein, HNP36	121	(-156)T>G	5
X97370	X97370	601459	4BB GEN-	H.sapiens mRNA for prepronociceptin	167	144T>C	S
X97370	X97370	601459	4BM GEN-	H.sapiens mRNA for prepronociceptin	637	614C>A	3
X97370	X97370	601459	4BM GEN-	H.sapiens mRNA for prepronociceptin	862	839C>G	3
Y00052	Y00052	123840	4BM GEN-SX	H.sapiens mRNA for prepronociceptin	221	207C>G	S
Y00052	Y00052	123840	GEN-SX	Cyclophilin A	268	254A>G	D85G
Y00052	Y00052	123840	GEN-SX	Cyclophilin A	332	318C>T	S
Y00052	Y00052	123840	GEN-SX	Cyclophilin A	627	613C>A	3
PTPRC	Y00062	151460	GEN-SY	Human mRNA for T200 leukocyte common antigen (CD45, LC-A)	3437	3291T>C	S
PTPRC	Y00062	151460	GEN-SY	Human mRNA for T200 leukocyte common antigen (CD45, LC-A)	3441	3295G>A	V1099I
Y00486	Y00486	102600	GEN-MGW	Human APRT gene for adenine	503	432C>A	S
Y00486	Y00486	102600	GEN-MGW	phosphoribosyltransferase Human APRT gene for adenine	505	434G>C	R145P
Y00486	Y00486	102600	GEN-MGW	phosphoribosyltransferase Human APRT gene for adenine	792	721A>G	3
Y00749	Y00749	131240	GEN-P7	phosphoribosyltransferase Endothelin 1	846	594G>T	K198N
TCRG	Y00790	186970	GEN-UC	Human mRNA for T-cell receptor gamma-chain	492	456G>A	S
TCRG	Y00790	186970	GEN-UC	Human mRNA for T-cell	507	471A>G	S

TCRG	Y00790	186970	GEN-UC	receptor gamma-chain Human mRNA for T-cell	528	492C>T	S
TCRG	Y00790	186970	GEN-UC	receptor gamma-chain Human mRNA for T-cell	555	519A>T	S
TCRG	Y00790	186970	GEN-UC	receptor gamma-chain Human mRNA for T-cell	559	523A>G	I175V
TCRG	Y00790	186970	GEN-UC	receptor gamma-chain Human mRNA for T-cell	636	600C>T	S
TCRG	Y00790	186970	GEN-UC	receptor gamma-chain Human mRNA for T-cell	676	640G>A	E214K
TCRG	Y00790	186970	GEN-UC	receptor gamma-chain Human mRNA for T-cell	733	697A>G	I233V
TCRG	Y00790	186970	GEN-UC	receptor gamma-chain Human mRNA for T-cell	849	813G>T	W271C
TCRG	Y00790	186970	GEN-UC	receptor gamma-chain Human mRNA for T-cell	908	872C>T	T291M
TCRG	Y00790	186970	GEN-UC	receptor gamma-chain Human mRNA for T-cell	970	934A>G	R312G
Y00796	Y00796	153370	GEN-2B	receptor gamma-chain Leukocyte integrin alpha-I	1006	918C>T	S
Y00796	Y00796	153370	GEN-2B	receptor gamma-chain Leukocyte integrin alpha-I	4519	4431A>G	3
CR1	Y00816	120620	GEN-UG	Human mRNA for complement receptor type 1 (CR1, C3b/C4b receptor, CD35)	207	180G>C	E60D
Y07683	Y07683	600843	GEN-4F1	H.sapiens mRNA for P2X3 purinoceptor	717	552C>T	S
Y07683	Y07683	600843	GEN-4F1	H.sapiens mRNA for P2X3 purinoceptor	753	588A>G	S
Y09561	Y09561	None	GEN-4F4	H.sapiens mRNA for P2X7 receptor	835	809A>G	H270R
Y09561	Y09561	None	GEN-4F4	H.sapiens mRNA for P2X7 receptor	946	920G>A	R307Q
Y09561	Y09561	None	GEN-4F4	H.sapiens mRNA for P2X7 receptor	1068	1042G>A	A348T
Y09561	Y09561	None	GEN-4F4	H.sapiens mRNA for P2X7 receptor	1096	1070C>G	T357S
Y09561	Y09561	None	GEN-4F4	H.sapiens mRNA for P2X7 receptor	1405	1379A>G	Q460R
Y09561	Y09561	None	GEN-4F4	H.sapiens mRNA for P2X7 receptor	1589	1563C>G	H521Q

Y09561	Y09561	None	GEN-4F4	H.sapiens mRNA for P2X7 receptor	1590	1564G>A	V522I
Y09561	Y09561	None	GEN-4F4	H.sapiens mRNA for P2X7 receptor	1628	1602G>T	S
Y09561	Y09561	None	GEN-4F4	H.sapiens mRNA for P2X7 receptor	1759	1733G>A	R578Q
Y09561	Y09561	None	GEN-4F4	H.sapiens mRNA for P2X7 receptor	1772	1746G>A	S
Y10659	Y10659	300119	GEN-1J6	H.sapiens IL-13Ra mRNA	1116	1073G>A	G358D
Y12509	Y12509	None	GEN-1ME	Homo sapiens mRNA for UDP-Gal:GlcNAc galactosyltransferase	257	257G>A	G86D
Y12510	Y12510	None	GEN-1MC	Homo sapiens mRNA for UDPGal:GlcNAc b1,4 galactosyltransferase	909	909C>T	S
Z11695	Z11695	176948	GEN-1L1	H.sapiens 40 kDa protein kinase related to rat ERK2	1287	1153G>A	3
Z11696	Z11696	601795	GEN-1L0	H.sapiens 44kDa protein kinase related to rat ERK1	449	449T>G	I150S
Z15108	Z15108	176982	GEN-1TE	H.sapiens mRNA for protein kinase C zeta	246	240T>C	S
Z15108	Z15108	176982	GEN-1TE	H.sapiens mRNA for protein kinase C zeta	1694	1688A>C	D563A
Z15108	Z15108	176982	GEN-1TE	H.sapiens mRNA for protein kinase C zeta	2033	2027G>A	3
Z15108	Z15108	176982	GEN-1TE	H.sapiens mRNA for protein kinase C zeta	2086	2080T>G	3
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B35 mRNA	25	25G>C	V9L
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B35 mRNA	103	103G>T	A35S
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B35 mRNA	106	106A>G	M36V
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B35 mRNA	165	165C>G	S
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B35 mRNA	209	209A>C	E70A
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B35 mRNA	213	213C>G	S
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B35 mRNA	222	222A>G	S
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B35 mRNA	259	259A>G	N87D
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B35 mRNA	261	261C>G	N87K
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B35 mRNA	353	353T>C	I118T
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B35 mRNA	355	355A>C	I119L
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B35 mRNA	362	362G>C	R121T

Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	379	379C>G	L127V
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	387	387C>G	S
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	409	409C>T	H137Y
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	412	412G>A	D138N
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	435	435G>A	S
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	463	463A>C	S155R
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	477	477G>C	S
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	486	486C>G	S
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	527	527T>A	V176E
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	538	538C>T	R180W
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	539	539G>T	R180L
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	544	544G>A	A182T
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	572	572G>C	W191S
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	583	583T>C	Y195H
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	603	603G>C	E201D
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	610	610C>G	Q204E
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	621	621C>A	D207E
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	623	623C>A	P208H
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	636	636C>T	S
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	648	648C>T	S
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	652	652G>A	V218I
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	668	668C>T	A223V
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	693	693C>T	S
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	756	756T>C	S
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	774	774A>G	S
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	786	786T>C	S
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	846	846A>G	S
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	900	900A>G	S
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	909	909G>A	S
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	916	916A>G	I306V
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	985	985A>G	T329A
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	1008	1008C>T	S
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	1046	1046C>G	S349C
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	1120	1120T>C	3
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	1164	1164G>A	3
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B*35 mRNA	1192	1192C>T	3

Z22651	Z22651	None	GEN-268	H.sapiens HLA-B35 mRNA	1209	1209C>T	3
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B35 mRNA	1219	1219C>A	3
Z22651	Z22651	None	GEN-268	H.sapiens HLA-B35 mRNA	1163	1135G>A	V379I
TAP2	Z22935	170261	GEN-26P	H.sapiens TAP2B mRNA, complete CDS	1186	1158G>T	S
TAP2	Z22935	170261	GEN-26P	H.sapiens TAP2B mRNA, complete CDS	1840	1812G>A	S
TAP2	Z22935	170261	GEN-26P	H.sapiens TAP2B mRNA, complete CDS	2021	1993G>A	A665T
TAP2	Z22935	170261	GEN-26P	H.sapiens TAP2B mRNA, complete CDS	2087	2059C>T	F
TAP2	Z22935	170261	GEN-26P	H.sapiens TAP2B mRNA, complete CDS	2119	2091T>G	S
HLA-DMB	Z23139	142856	GEN-277	H.sapiens RING7 mRNA for HLA class II alpha chain-like product	380	212G>A	S71N
HLA-DMB	Z23139	142856	GEN-277	H.sapiens RING7 mRNA for HLA class II alpha chain-like product	1125	957C>T	3
Z26649	Z26649	600230	GEN-2B5	Phospholipase C beta-3	437	438C>T	3
Z26649	Z26649	600230	GEN-2B5	Phospholipase C beta-3	466	467G>A	3
Z26649	Z26649	600230	GEN-2B5	Phospholipase C beta-3	2664	2665C>T	3
Z26649	Z26649	600230	GEN-2B5	Phospholipase C beta-3	3168	3169G>T	3
ECE1	Z35307	600423	GEN-2MA	Endothelin Converting Enzyme 1	1141	1104C>T	S
ECE1	Z35307	600423	GEN-2MA	Endothelin Converting Enzyme 1	1627	1590T>C	S
ECE1	Z35307	600423	GEN-2MA	Endothelin Converting Enzyme 1	1696	1659G>A	S
ECE1	Z35307	600423	GEN-2MA	Endothelin Converting Enzyme 1	1946	1909G>A	V637M
ECE1	Z35307	600423	GEN-2MA	Endothelin Converting Enzyme 1	2433	2396G>A	3
Z35491	Z35491	601497	GEN-2ME	H.sapiens mRNA for novel glucocorticoid receptor-	315	37G>A	E13K

Z35491	Z35491	601497	GEN-2ME	H.sapiens mRNA for novel glucocorticoid receptor-associated protein	333	55G>A	E19K
Z35491	Z35491	601497	GEN-2ME	H.sapiens mRNA for novel glucocorticoid receptor-associated protein	1297	1019A>C	3
PDE4C	Z46632	600128	GEN-2X2	H.sapiens HSPDE4C1 gene for 3,5-cyclic AMP phosphodiesterase	280	169C>T	R57C
PDE4C	Z46632	600128	GEN-2X2	H.sapiens HSPDE4C1 gene for 3,5-cyclic AMP phosphodiesterase	1142	1031G>A	R344Q
Z48810	Z48810	602664	GEN-2YJ	H.sapiens mRNA for TX protease precursor	1280	1239A>C	3
Z56281	Z56281	603734	GEN-36V	H.sapiens mRNA for interferon regulatory factor	883	837G>A	S
Z56281	Z56281	603734	GEN-36V	H.sapiens mRNA for interferon regulatory factor	1114	1068G>A	S
Z56281	Z56281	603734	GEN-36V	H.sapiens mRNA for interferon regulatory factor	1175	1129G>A	E377K
Z56281	Z56281	603734	GEN-36V	H.sapiens mRNA for interferon regulatory factor	1326	1280G>C	S427T
Z56281	Z56281	603734	GEN-36V	H.sapiens mRNA for interferon regulatory factor	1373	1327A>C	3

Table 16.
Identified
Variances
In Genes
for
Pathways
Identified
in
Endocrine
and

SD-144146.1

Metabolic
Disease

AB00026	3	AB00026	602784	GEN-16N	Human mRNA for prepro cortistatin like peptide, complete cds	215	210T>C	S
AB00238	5	AB00238	601698	GEN-1D6	Human mRNA for KIAA0387 gene, partial cds	612	612A>G	S
AB00238	5	AB00238	601698	GEN-1D6	Human mRNA for KIAA0387 gene, partial cds	628	628A>G	T210A
AB00238	5	AB00238	601698	GEN-1D6	Human mRNA for KIAA0387 gene, partial cds	871	871T>C	+291Q
AB00238	5	AB00238	601698	GEN-1D6	Human mRNA for KIAA0387 gene, partial cds	948	948G>A	S
AB00238	5	AB00238	601698	GEN-1D6	Human mRNA for KIAA0387 gene, partial cds	973	973T>C	+325R
AB00238	5	AB00238	601698	GEN-1D6	Human mRNA for KIAA0387 gene, partial cds	1600	1600C>T	R534C
AB00238	5	AB00238	601698	GEN-1D6	Human mRNA for KIAA0387 gene, partial cds	2308	2308T>C	C770R
AB00238	5	AB00238	601698	GEN-1D6	Human mRNA for KIAA0387 gene, partial cds	2770	2770G>A	V924M
AB00238	5	AB00238	601698	GEN-1D6	Human mRNA for KIAA0387 gene, partial cds	3727	3727G>A	3
AB00238	5	AB00238	601698	GEN-1D6	Human mRNA for KIAA0387 gene, partial cds	4036	4036G>A	3
AB00238	5	AB00238	601698	GEN-1D6	Human mRNA for KIAA0387 gene, partial cds	4602	4602C>A	3
AB00238	5	AB00238	601698	GEN-1D6	Human mRNA for KIAA0387 gene, partial cds	4621	4621C>A	3
AB00528	9	AB00528	300135	GEN-KVU	Homo sapiens mRNA for ABC transporter 7 protein, complete cds	2137	2069A>T	H690L
AB00529	3	AB00529	170290	GEN-W4	Homo sapiens mRNA for perlipin, complete cds	2197	2073A>T	3
AB00942	6	AB00942	600130	GEN-MDN	Homo sapiens gene for apobec-1	1016	534C>T	S
AB01071	0	AB01071	602601	GEN-1SQ	Homo sapiens mRNA for lectin-like oxidized LDL receptor, complete cds	1071	1010T>A	3
AB01071	0	AB01071	602601	GEN-	Homo sapiens mRNA for	1073	1012T>C	3

0	0	1SQ	lectin-like oxidized LDL receptor, complete cds	1073	1012T>C	3
AB01071	AB01071	GEN-1SQ	Homo sapiens mRNA for lectin-like oxidized LDL receptor, complete cds	1801	1740A>G	3
AB01071	AB01071	GEN-1SQ	Homo sapiens mRNA for lectin-like oxidized LDL receptor, complete cds	2199	2138G>A	3
AB01071	AB01071	GEN-1SQ	Homo sapiens mRNA for lectin-like oxidized LDL receptor, complete cds	249	213T>C	S
AB01336	AB01336	GEN-L6C	DPM2, complete cds	263	227C>G	T76S
AB01336	AB01336	GEN-L6C	DPM2, complete cds	2468	2369G>A	3
AB01678	AB01678	GEN-L39	Homo sapiens mRNA for Glutamine:fructose-6-phosphate amidotransferase, complete cds	2549	2450G>A	3
AB01678	AB01678	GEN-L39	Homo sapiens mRNA for Glutamine:fructose-6-phosphate amidotransferase, complete cds	2755	2656G>A	3
AB01678	AB01678	GEN-L39	Homo sapiens mRNA for Glutamine:fructose-6-phosphate amidotransferase, complete cds	3998	3914G>T	3
ACLY	X64330	GEN-3F0	H.sapiens mRNA for ATP-citrate lyase	4229	4145A>C	3
ACLY	X64330	GEN-3F0	H.sapiens mRNA for ATP-citrate lyase	1044	1038T>C	S
AF001174	AF001174	GEN-18T	Homo sapiens p38beta2 MAP kinase mRNA, complete cds	75	67T>C	C23R
AF001437	AF001437	GEN-9T	Dihydrolipoamide S-acetyltransferase (E2 component of pyruvate dehydrogenase complex)			

AF001437	AF001437	245349	GEN-9T	Dihydrolipoamide S- acetyltransferase (E2 component of pyruvate dehydrogenase complex)	116	108C>T	S
AF001437	AF001437	245349	GEN-9T	Dihydrolipoamide S- acetyltransferase (E2 component of pyruvate dehydrogenase complex)	759	751T>G	S251A
AF001437	AF001437	245349	GEN-9T	Dihydrolipoamide S- acetyltransferase (E2 component of pyruvate dehydrogenase complex)	806	798C>T	S
AF001437	AF001437	245349	GEN-9T	Dihydrolipoamide S- acetyltransferase (E2 component of pyruvate dehydrogenase complex)	866	858T>C	S
AF001437	AF001437	245349	GEN-9T	Dihydrolipoamide S- acetyltransferase (E2 component of pyruvate dehydrogenase complex)	2000	1992G>T	3
AF001437	AF001437	245349	GEN-9T	Dihydrolipoamide S- acetyltransferase (E2 component of pyruvate dehydrogenase complex)	2158	2150C>A	3
AF004709	AF004709	602899	GEN-UX	Homo sapiens stress- activated protein kinase 4 mRNA, complete cds	432	384G>A	S
AF009923	AF009923	603169	GEN- KZM	Homo sapiens preprocathepsin P mRNA, partial cds	702	702C>T	S
AF009923	AF009923	603169	GEN- KZM	Homo sapiens preprocathepsin P mRNA, partial cds	1018	1018T>C	3
AF009923	AF009923	603169	GEN- KZM	Homo sapiens preprocathepsin P mRNA, partial cds	1129	1129G>A	3
AF013611	AF013611	602364	GEN- 20Z	Homo sapiens lymphopain mRNA, complete cds	537	537T>G	H179Q
AF030625	AF030625	600821	GEN-2	Vasopressin V1A receptor	314	291C>T	S
AF030625	AF030625	600821	GEN-2	Vasopressin V1A receptor	431	408T>C	S
AF030625	AF030625	600821	GEN-2	Vasopressin V1A receptor	506	483A>G	S

AF053712	AF053712	None	GEN- MM2	Homo sapiens osteoprotegerin ligand mRNA, complete cds	2086	1902T>G	3
AF064548	AF064548	603506	GEN- KV4	Homo sapiens low-density lipoprotein receptor-related protein 5 (LRP5) mRNA, complete cds	1695	1647C>T	S
AF064548	AF064548	603506	GEN- KV4	Homo sapiens low-density lipoprotein receptor-related protein 5 (LRP5) mRNA, complete cds	4037	3989C>T	A1330V
AF064548	AF064548	603506	GEN- KV4	Homo sapiens low-density lipoprotein receptor-related protein 5 (LRP5) mRNA, complete cds	4683	4635C>A	S
AF064548	AF064548	603506	GEN- KV4	Homo sapiens low-density lipoprotein receptor-related protein 5 (LRP5) mRNA, complete cds	4802	4754C>T	S1585L
AF066859	AF066859	232600	GEN- LKT	Homo sapiens muscle glycogen phosphorylase (PYGM) mRNA, complete cds	53	53G>A	G18D
AF066859	AF066859	232600	GEN- LKT	Homo sapiens muscle glycogen phosphorylase (PYGM) mRNA, complete cds	856	856T>C	F286L
AF066859	AF066859	232600	GEN- LKT	Homo sapiens muscle glycogen phosphorylase (PYGM) mRNA, complete cds	1716	1716C>T	S
AF071748	AF071748	None	GEN- LOZ	Homo sapiens cathepsin F (CATSF) mRNA, complete cds	1055	963C>T	S
AF071748	AF071748	None	GEN- LOZ	Homo sapiens cathepsin F (CATSF) mRNA, complete cds	1344	1252G>A	3
AF071748	AF071748	None	GEN- LOZ	Homo sapiens cathepsin F (CATSF) mRNA, complete cds	1513	1421T>C	3
AF071748	AF071748	None	GEN- LOZ	Homo sapiens cathepsin F (CATSF) mRNA, complete cds	1574	1482C>A	3

AF071748	AF071748	None	LOZ	(CATSF) mRNA, complete cds	1576	1484G>A	3
			GEN- LOZ	Homo sapiens cathepsin F (CATSF) mRNA, complete cds			
AGL	U84007	232400	GEN- 3Z7	Human glycogen debranching enzyme isoform 1 (AGL) mRNA, alternatively spliced isoform, complete cds	7309	6909A>G	3
AGT	K02215	106150	GEN-WK	Human angiotensinogen mRNA, complete CDS	659	620C>T	T207M
AGT	K02215	106150	GEN-WK	Human angiotensinogen mRNA, complete CDS	842	803T>C	M268T
AGT	K02215	106150	GEN-WK	Human angiotensinogen mRNA, complete CDS	1155	1116G>A	S
AGT	K02215	106150	GEN-WK	Human angiotensinogen mRNA, complete CDS	1476	1437C>A	S
AGT	K02215	106150	GEN-WK	Human angiotensinogen mRNA, complete CDS	1821	1782G>A	3
AGT	K02215	106150	GEN-WK	Human angiotensinogen mRNA, complete CDS	2053	2014A>C	3
AJ005162	AJ005162	600067	GEN- KVT	Homo sapiens mRNA for UDP-glucuronosyltransferase	1915	1882A>C	3
APOH	M62839	138700	GEN- 3CY	Human apolipoprotein H mRNA, complete cds	500	461G>A	R154H
APOH	M62839	138700	GEN- 3CY	Human apolipoprotein H mRNA, complete cds	835	796G>T	V266L
APOH	M62839	138700	GEN- 3CY	Human apolipoprotein H mRNA, complete cds	1098	1059T>C	3
ARG1	M14502	207800	GEN- 1RE	Human liver arginase mRNA, complete cds	800	744C>T	S
AVPR1B	AF030512	600264	GEN- 4FF	Homo sapiens small cell vasopressin subtype 1b receptor mRNA, complete cds	273	150G>A	S
BMP1	M22488	112264	GEN- 25X	Human bone morphogenetic protein 1 (BMP-1) mRNA	2224	2195G>A	3
BMP4	M22490	112262	GEN-	Human bone	849	455T>C	V152A

BNSDOCID: <WO 0050639A2 | >

CETP	M30185	118470	GEN-2FK	Human cholesteryl ester transfer protein mRNA, complete cds	1696	1566G>A	3
CLU	X14723	185430	GEN-1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	131	84C>T	S
CLU	X14723	185430	GEN-1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	429	382G>T	V128F
CLU	X14723	185430	GEN-1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	836	789C>T	S
CLU	X14723	185430	GEN-1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	1234	1187C>T	S396L
CLU	X14723	185430	GEN-1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	1372	1325A>T	Y442F
CLU	X14723	185430	GEN-1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	1482	1435C>T	3
CLU	X14723	185430	GEN-1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	1548	1501C>T	3
CLU	X14723	185430	GEN-1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	1645	1598A>T	3
COL18A1	L22548	120328	GEN-262	Human collagen type XVIII alpha 1 (COL18A1) mRNA, partial cds	22	22A>G	I8V
COL18A1	L22548	120328	GEN-262	Human collagen type XVIII alpha 1 (COL18A1) mRNA, partial cds	2071	2071A>G	3

COL18A1	L22548	120328	GEN-262	Human collagen type XVIII alpha 1 (COL18A1) mRNA, partial cds	2126	2126A>G	3
COL18A1	L22548	120328	GEN-262	Human collagen type XVIII alpha 1 (COL18A1) mRNA, partial cds	2395	2395A>G	3
COL18A1	L22548	120328	GEN-262	Human collagen type XVIII alpha 1 (COL18A1) mRNA, partial cds	3372	3372A>T	3
COL18A1	L22548	120328	GEN-262	Human collagen type XVIII alpha 1 (COL18A1) mRNA, partial cds	3374	3374A>C	3
CRHBP	X58022	122559	GEN-38K	Human mRNA for corticotropin-releasing factor binding protein (CRF-BP)	987	941T>G	I314S
CTGF	U14750	121009	GEN-1S3	Human connective tissue growth factor mRNA, partial cds	1878	1878A>C	3
CTSG	M16117	116830	GEN-1XI	Human cathepsin G mRNA, complete cds	382	374A>G	N125S
CTSL	X12451	116880	GEN-1M1	Human mRNA for pro- cathepsin L (major excreted protein MEP)	1300	1012C>T	3
CYP11B2	D13752	124080	GEN-CCD	Human CYP11B2 gene for steroid 18-hydroxylase, complete cds	1600	1593G>A	3
CYP21	M17252	201910	GEN-201	Human cytochrome P450c21 mRNA, 3 end	224	224G>A	R75H
CYP21	M17252	201910	GEN-201	Human cytochrome P450c21 mRNA, 3 end	330	330C>T	S
CYP21	M17252	201910	GEN-201	Human cytochrome P450c21 mRNA, 3 end	745	745T>C	3
D13811	D13811	238310	GEN-AA	Glycine cleavage system: Protein T	277	148G>T	V50L
D13811	D13811	238310	GEN-AA	Glycine cleavage system: Protein T	1073	944G>A	R315K
D13811	D13811	238310	GEN-AA	Glycine cleavage system: Protein T	1083	954G>A	S
D13811	D13811	238310	GEN-AA	Glycine cleavage system: Protein T	1773	1644C>T	3

D13811	D13811	238310	GEN-AA	Protein T Glycine cleavage system: Protein T	2037	1908C>T	3
D50678	D50678	602600	GEN-30Y	Human mRNA for apolipoprotein E receptor 2, complete cds	3378	3276G>A	3
D50678	D50678	602600	GEN-30Y	Human mRNA for apolipoprotein E receptor 2, complete cds	3755	3653G>A	3
D50678	D50678	602600	GEN-30Y	Human mRNA for apolipoprotein E receptor 2, complete cds	3949	3847G>C	3
D50678	D50678	602600	GEN-30Y	Human mRNA for apolipoprotein E receptor 2, complete cds	4368	4266T>A	3
D50678	D50678	602600	GEN-30Y	Human mRNA for apolipoprotein E receptor 2, complete cds	4455	4353G>A	3
D63480	D63480	116898	GEN-3DN	Human mRNA for KIAA0146 gene, partial cds	1728	1728G>A	S
D82347	D82347	601724	GEN-MIP	Neurogenic differentiation 1	804	695G>A	G232D
D85730	D85730	140559	GEN-LR0	Homo sapiens HSPA1L mRNA for Heat shock protein 70 testis variant, complete cds	2156	2021C>G	3
D87258	D87258	602194	GEN-42R	Homo sapiens mRNA for serin protease with IGF-binding motif, complete cds	150	102C>T	S
D87812	D87812	600528	GEN-6	Palmitoyltransferase I (muscle) ACAT1	2363	2344T>C	3
D90228	D90228	203750	GEN-46A	Human chondroitin/dermatan sulfate proteoglycan (PG40) core protein mRNA, complete cds	547	471C>A	S
DCN	M14219	125255	GEN-1QX	Human chondroitin/dermatan	1490	1409A>G	3
DCN	M14219	125255	GEN-1QX	Human chondroitin/dermatan	1534	1453C>T	3

DRD1	X58987	126449	GEN-4EH	sulfate proteoglycan (PG40) core protein mRNA, complete cds	D1 dopaminergic receptor	229	(-48)A>G	5
DRD1	X58987	126449	GEN-4EH		D1 dopaminergic receptor	366	90G>A	S
DRD1	X58987	126449	GEN-4EH		D1 dopaminergic receptor	474	198G>A	S
DRD1	X58987	126449	GEN-4EH		D1 dopaminergic receptor	1539	1263G>A	S
DRD1	X58987	126449	GEN-4EH		D1 dopaminergic receptor	2040	1764A>C	3
DRD1	X58987	126449	GEN-4EH		D1 dopaminergic receptor	2045	1769C>A	3
ECE1	Z35307	600423	GEN-2MA		Endothelin Converting Enzyme 1	1141	1104C>T	S
ECE1	Z35307	600423	GEN-2MA		Endothelin Converting Enzyme 1	1627	1590T>C	S
ECE1	Z35307	600423	GEN-2MA		Endothelin Converting Enzyme 1	1696	1659G>A	S
ECE1	Z35307	600423	GEN-2MA		Endothelin Converting Enzyme 1	1946	1909G>A	V637M
ECE1	Z35307	600423	GEN-2MA		Endothelin Converting Enzyme 1	2433	2396G>A	3
EDN2	M65199	131241	GEN-CBS		Endothelin 2	384	314C>T	A105V
EDN2	M65199	131241	GEN-CBS		Endothelin 2	997	927A>G	3
EDN2	M65199	131241	GEN-CBS		Endothelin 2	997	927A>G	3
EDN3	X52001	131242	GEN-33E		Endothelin 3	1262	1152G>A	3
EDN3	X52001	131242	GEN-33E		Endothelin 3	1649	1539C>G	3
EDN3	X52001	131242	GEN-33E		Endothelin 3	1700	1590C>T	3
EDN3	X52001	131242	GEN-33E		Endothelin 3	1742	1632C>T	3
EDN3	X52001	131242	GEN-33E		Endothelin 3	1797	1687C>T	3

EDN3	X52001	131242	GEN-33E	Endothelin 3	1914	1804G>C	3
EDN3	X52001	131242	GEN-33E	Endothelin 3	2040	1930C>T	3
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	1449	969C>T	S
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	1449	969C>T	S
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	1485	1005A>G	S
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	1485	1005A>G	S
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	1834	1354C>G	3
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	1834	1354C>G	3
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	2228	1748G>A	3
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	2376	1896G>A	3
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	2764	2284G>A	3
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	2764	2284G>A	3
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	2840	2360G>C	3
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	2935	2455G>A	3
EDNRA	D90348	131243	GEN-4DX	Endothelin Receptor Type A	3294	2814A>G	3
EDNRB	L06623	131244	GEN-19S	Endothelin Receptor Type B	88	(-146)A>G	5
EDNRB	L06623	131244	GEN-19S	Endothelin Receptor Type B	332	99C>T	S
EDNRB	L06623	131244	GEN-19S	Endothelin Receptor Type B	1064	831G>A	S
EDNRB	L06623	131244	GEN-19S	Endothelin Receptor Type B	1064	831G>A	S
EHHADH	L07077	261515	GEN-1DF	Human enoyl-CoA: hydratase 3-hydroxyacyl-CoA dehydrogenase	1225	1218G>A	S

EHHADH	L07077	261515	GEN-1DF	(EHHADH) mRNA, complete cds with repeats Human enoyl-CoA hydratase 3-hydroxyacyl-CoA dehydrogenase (EHHADH) mRNA, complete cds with repeats	1823	1816C>A	P606T
FACL1	L09229	152425	GEN-1GI	Human long-chain acyl-coenzyme A synthetase (FACL1) mRNA, complete cds	3026	2953G>A	3
FACL1	L09229	152425	GEN-1GI	Human long-chain acyl-coenzyme A synthetase (FACL1) mRNA, complete cds	3083	3010G>A	3
FGF7	M60828	148180	GEN-3BE	Human keratinocyte growth factor mRNA, complete cds	323	(-123)G>C	5
FGF7	M60828	148180	GEN-3BE	Human keratinocyte growth factor mRNA, complete cds	1180	735T>C	3
FGF7	M60828	148180	GEN-3BE	Human keratinocyte growth factor mRNA, complete cds	1201	756A>G	3
FGF7	M60828	148180	GEN-3BE	Human keratinocyte growth factor mRNA, complete cds	1216	771A>G	3
FGF7	M60828	148180	GEN-3BE	Human keratinocyte growth factor mRNA, complete cds	1218	773G>C	3
FGF7	M60828	148180	GEN-3BE	Human keratinocyte growth factor mRNA, complete cds	1266	821A>C	3
FGF7	M60828	148180	GEN-3BE	Human keratinocyte growth factor mRNA, complete cds	1306	861C>T	3
FGF7	M60828	148180	GEN-3BE	Human keratinocyte growth factor mRNA, complete cds	1654	1209A>T	3
FGF7	M60828	148180	GEN-3BE	Human keratinocyte growth factor mRNA, complete cds	1657	1212T>C	3

FGF7	M60828	148180	GEN-3BE	complete cds Human keratinocyte growth factor mRNA,	1799	1354A>T	3
FGF7	M60828	148180	GEN-3BE	complete cds Human keratinocyte growth factor mRNA,	1801	1356C>T	3
FGF7	M60828	148180	GEN-3BE	complete cds Human keratinocyte growth factor mRNA,	1867	1422A>G	3
FGF7	M60828	148180	GEN-3BE	complete cds Human keratinocyte growth factor mRNA,	1945	1500C>A	3
FGF7	M60828	148180	GEN-3BE	complete cds Human keratinocyte growth factor mRNA,	1973	1528G>A	3
FGF7	M60828	148180	GEN-3BE	complete cds Human keratinocyte growth factor mRNA,	2167	1722G>A	3
FGF7	M60828	148180	GEN-3BE	complete cds Human keratinocyte growth factor mRNA,	2186	1741A>G	3
FGF7	M60828	148180	GEN-3BE	complete cds Human keratinocyte growth factor mRNA,	2302	1857T>A	3
FGF7	M60828	148180	GEN-3BE	complete cds Human keratinocyte growth factor mRNA,	2328	1883G>A	3
FGF8	U36223	600483	GEN-2MX	complete cds Human fibroblast growth factor 8 (FGF-8) mRNA,	300	291T>C	S
FGF8	U36223	600483	GEN-2MX	complete cds Human fibroblast growth factor 8 (FGF-8) mRNA,	645	636G>C	S
FGF8	U36223	600483	GEN-2MX	complete cds Human fibroblast growth factor 8 (FGF-8) mRNA,	648	639A>G	S
FGFR1	X51803	136350	GEN-32G	complete cds Human mRNA for fibroblast growth factor (FGF) receptor	276	159T>G	S
FGFR2	X52832	176943	GEN-341	Human bek mRNA for	338	159A>G	S

FGFR2	X52832	176943	GEN-341	fibroblast growth factor receptor-BEK	2903	2724A>T	3
				Human bek mRNA for fibroblast growth factor receptor-BEK			
FGFR3	M64347	134934	GEN-3EX	Human novel growth factor receptor mRNA, 3 cds	3108	3108C>A	3
FGFR3	M64347	134934	GEN-3EX	Human novel growth factor receptor mRNA, 3 cds	3715	3715G>A	3
FGFR4	X57205	134935	GEN-37M	Human FGFR-4 mRNA for fibroblast growth factor receptor (FGFR-4)	83	28G>A	V10I
FGFR4	X57205	134935	GEN-37M	Human FGFR-4 mRNA for fibroblast growth factor receptor (FGFR-4)	217	162T>G	S
FSHR	M65085	136435	GEN-3FQ	FSH receptor	2105	2039G>A	S680N
GAA	Y00839	232300	GEN-UJ	a-glucosidase	815	(-14)G>A	5
GAA	Y00839	232300	GEN-UJ	a-glucosidase	861	33C>T	S
GAA	Y00839	232300	GEN-UJ	a-glucosidase	3301	2473C>T	3
GAA	Y00839	232300	GEN-UJ	a-glucosidase	3477	2649C>T	3
GAA	Y00839	232300	GEN-UJ	a-glucosidase	3496	2668T>G	3
GAA	Y00839	232300	GEN-UJ	a-glucosidase	3509	2681G>A	3
GALN	M77140	137035	GEN-3PM	H.sapiens pro-galanin mRNA, 3 end	339	339C>T	3
GC	M12654	139200	GEN-1MN	Human serum vitamin D-binding protein (hDBP) mRNA, complete cds	925	897T>C	S
GC	M12654	139200	GEN-1MN	Human serum vitamin D-binding protein (hDBP) mRNA, complete cds	1324	1296G>T	E432D
GC	M12654	139200	GEN-1MN	Human serum vitamin D-binding protein (hDBP) mRNA, complete cds	1335	1307C>A	T436K
GC	M12654	139200	GEN-1MN	Human serum vitamin D-binding protein (hDBP) mRNA, complete cds	1362	1334G>A	R445H
GLP1R	U01157	138032	GEN-V3	Human glucagon-like peptide-1 receptor mRNA with CA dinucleotide	780	780C>A	F260L

GLP1R	U01157	138032	GEN-V3	repeat, complete cds Human glucagon-like peptide-1 receptor mRNA with CA dinucleotide	780	780C>A	F260L
GLP1R	U01157	138032	GEN-V3	repeat, complete cds Human glucagon-like peptide-1 receptor mRNA with CA dinucleotide	947	947G>C	G316A
GLP1R	U01157	138032	GEN-V3	repeat, complete cds Human glucagon-like peptide-1 receptor mRNA with CA dinucleotide	947	947G>C	G316A
GLP1R	U01157	138032	GEN-V3	repeat, complete cds Human glucagon-like peptide-1 receptor mRNA with CA dinucleotide	1200	1200C>A	S
GLP1R	U01157	138032	GEN-V3	repeat, complete cds Human glucagon-like peptide-1 receptor mRNA with CA dinucleotide	1200	1200C>A	S
GNRHR	L07949	138850	GEN-1F1	repeat, complete cds Gonadotropin releasing hormone agonist	1371	1347C>A	3
GPX1	Y00433	138320	GEN-TJ	Human mRNA for glutathione peroxidase (EC 1.11.1.9.)	504	186G>A	S
GPX1	Y00433	138320	GEN-TJ	Human mRNA for glutathione peroxidase (EC 1.11.1.9.)	610	292C>G	R98G
GPX1	Y00433	138320	GEN-TJ	Human mRNA for glutathione peroxidase (EC 1.11.1.9.)	911	593C>T	P198L
GPX1	Y00433	138320	GEN-TJ	Human mRNA for glutathione peroxidase (EC 1.11.1.9.)	1048	730A>C	3
GPX1	Y00433	138320	GEN-TJ	Human mRNA for glutathione peroxidase (EC 1.11.1.9.)	1110	792A>C	3
GPX3	X58295	138321	GEN-38S	Human GPx-3 mRNA for plasma glutathione peroxidase	821	773C>T	3

GPX3	X58295	138321	GEN-38S	Human GPx-3 mRNA for plasma glutathione peroxidase	979	931G>A	3
GPX3	X58295	138321	GEN-38S	Human GPx-3 mRNA for plasma glutathione peroxidase	1187	1139T>G	3
GPX3	X58295	138321	GEN-38S	Human GPx-3 mRNA for plasma glutathione peroxidase	1354	1306C>T	3
GPX3	X58295	138321	GEN-38S	Human GPx-3 mRNA for plasma glutathione peroxidase	1443	1395C>T	3
GPX3	X58295	138321	GEN-38S	Human GPx-3 mRNA for plasma glutathione peroxidase	1516	1468C>A	3
GPX3	X58295	138321	GEN-38S	Human GPx-3 mRNA for plasma glutathione peroxidase	1581	1533C>T	3
GPX4	X71973	138322	GEN-3L1	H.sapiens GPx-4 mRNA for phospholipid hydroperoxide glutathione peroxidase	718	638T>C	3
GPX4	X71973	138322	GEN-3L1	H.sapiens GPx-4 mRNA for phospholipid hydroperoxide glutathione peroxidase	837	757C>A	3
GPX4	X71973	138322	GEN-3L1	H.sapiens GPx-4 mRNA for phospholipid hydroperoxide glutathione peroxidase	882	802A>C	3
GSS	U34683	601002	GEN-2LF	Human glutathione synthetase mRNA, complete cds	364	324G>A	S
GYS1	J04501	138570	GEN-14W	Human muscle glycogen synthase mRNA, complete cds	567	407T>C	I136T
GYS1	J04501	138570	GEN-14W	Human muscle glycogen synthase mRNA, complete cds	2276	2116C>A	R706S
GYS1	J04501	138570	GEN-14W	Human muscle glycogen synthase mRNA, complete cds	2457	2297A>C	3

GYS1	J04501	138570	GEN-14W	Human muscle glycogen synthase mRNA, complete cds	2470	2310C>T	3
GYS1	J04501	138570	GEN-14W	Human muscle glycogen synthase mRNA, complete cds	3099	2939T>C	3
HADHA	U04627	600890	GEN-155	Human 78 kDa gastrin-binding protein mRNA, complete cds	1507	1507G>A	V503M
HADHB	D16481	143450	GEN-1Y5	Human mRNA for mitochondrial 3-ketoacyl-CoA thiolase beta-subunit of trifunctional protein, complete cds	871	825T>C	S
HADHB	D16481	143450	GEN-1Y5	Human mRNA for mitochondrial 3-ketoacyl-CoA thiolase beta-subunit of trifunctional protein, complete cds	1607	1561G>C	3
HADHB	D16481	143450	GEN-1Y5	Human mRNA for mitochondrial 3-ketoacyl-CoA thiolase beta-subunit of trifunctional protein, complete cds	1908	1862A>C	3
HADHB	D16481	143450	GEN-1Y5	Human mRNA for mitochondrial 3-ketoacyl-CoA thiolase beta-subunit of trifunctional protein, complete cds	1911	1865A>C	3
HGF	X16323	142409	GEN-1Y1	Human mRNA for hepatocyte growth factor (HGF)	5740	5606T>A	3
HSD17B3	U05659	264300	GEN-186	Human 17beta-hydroxysteroid dehydrogenase type 3 mRNA, complete cds	894	846G>C	S
IGFBP4	M62403	146733	GEN-3CJ	Human insulin-like growth factor binding protein 4 (IGFBP4) mRNA, complete cds	859	776G>A	S

IGFBP4	M62403	146733	GEN-3CJ	Human insulin-like growth factor binding protein 4 (IGFBP4) mRNA, complete cds	1403	1320G>T	3
IGFBP4	M62403	146733	GEN-3CJ	Human insulin-like growth factor binding protein 4 (IGFBP4) mRNA, complete cds	1443	1360G>A	3
IGFBP4	M62403	146733	GEN-3CJ	Human insulin-like growth factor binding protein 4 (IGFBP4) mRNA, complete cds	1446	1363G>A	3
IGFBP4	M62403	146733	GEN-3CJ	Human insulin-like growth factor binding protein 4 (IGFBP4) mRNA, complete cds	1485	1402A>T	3
IGFBP6	M69054	146735	GEN-3J0	Human insulin-like growth factor binding protein 6 (IGFBP6) mRNA, complete mature peptide	751	751A>C	3
IGFBP6	M69054	146735	GEN-3J0	Human insulin-like growth factor binding protein 6 (IGFBP6) mRNA, complete mature peptide	835	835A>C	3
IGFBP6	M69054	146735	GEN-3J0	Human insulin-like growth factor binding protein 6 (IGFBP6) mRNA, complete mature peptide	850	850G>A	3
ITGA5	X06256	135620	GEN-19B	Human mRNA for fibronectin receptor alpha subunit	2562	2539C>A	L847I
J00117	J00117	118860	GEN-2H	CHORIOGONADOTROPI N BETA CHAIN PRECURSOR	17	(-9)G>A	5
J00117	J00117	118860	GEN-2H	CHORIOGONADOTROPI N BETA CHAIN PRECURSOR	155	130C>A	P44T
J00117	J00117	118860	GEN-2H	CHORIOGONADOTROPI N BETA CHAIN PRECURSOR	331	306C>A	F
J00117	J00117	118860	GEN-2H	CHORIOGONADOTROPI N BETA CHAIN PRECURSOR	435	410A>C	D137A

J00117	J00117	118860	GEN-2H	CHORIOGONADOTROPI N BETA CHAIN PRECURSOR	475	450C>T	S
J00117	J00117	118860	GEN-2H	CHORIOGONADOTROPI N BETA CHAIN PRECURSOR	517	492A>C	S
J00123	J00123	131330	GEN- MK4	Human enkephalin gene	81	81C>T	S
J00277	J00277	190020	GEN- MH8	Human (genomic clones lambda-[SK2-T2, HS578T]; cDNA clones RS-[3, 4, 6]) c-Ha-ras1 proto-oncogene, complete coding sequence	81	81T>C	S
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	1931	1853T>C	V618A
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	6616	6538C>T	F
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	7014	6936T>C	S
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	7623	7545T>C	S
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	8294	8216C>T	P2739L
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	8625	8547T>C	S
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	10033	9955G>C	D3319H
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	10358	10280C>A	T3427K
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	10372	10294C>G	Q3432E
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	11273	11195T>C	I3732T
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	11705	11627C>T	A3876V
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	11862	11784T>A	S
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	11923	11845T>C	F3949L

J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	12461	12383A>T	E4128V
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	12476	12398G>C	G4133A
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	12486	12408G>C	S
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	12619	12541G>A	E4181K
J02611	J02611	107740	GEN-6O	Human apolipoprotein D mRNA, complete cds	676	615T>G	3
J02611	J02611	107740	GEN-6O	Human apolipoprotein D mRNA, complete cds	683	622T>G	3
J02611	J02611	107740	GEN-6O	Human apolipoprotein D mRNA, complete cds	701	640C>G	3
J02611	J02611	107740	GEN-6O	Human apolipoprotein D mRNA, complete cds	745	684A>G	3
J03209	J03209	185250	GEN-PK	Human matrix metalloproteinase-3 (MMP-3) mRNA, complete cds	133	133G>A	E45K
J03209	J03209	185250	GEN-PK	Human matrix metalloproteinase-3 (MMP-3) mRNA, complete cds	288	288C>T	S
J03210	J03210	120360	GEN-ZY	Human collagenase type IV mRNA, 3 end	721	721C>T	P241S
J03210	J03210	120360	GEN-ZY	Human collagenase type IV mRNA, 3 end	1759	1759C>T	P587S
J03242	J03242	147470	GEN-PJ	Insulin-like growth factor 2	932	380G>A	R127H
J03242	J03242	147470	GEN-PJ	Insulin-like growth factor 2	1063	511G>A	A171T
J03242	J03242	147470	GEN-PJ	Insulin-like growth factor 2	1190	638C>G	3
J03242	J03242	147470	GEN-PJ	Insulin-like growth factor 2	1201	649C>T	3
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	172	57C>T	S
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	559	444C>T	S
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	1704	1589C>A	3
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	1833	1718C>G	3

J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	1858	1743G>T	3
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	1959	1844A>C	3
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	2190	2075delT	F
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	3301	3186C>A	3
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	3991	3876A>G	3
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	4187	4072G>A	3
J03258	J03258	601769	GEN-2J	Vitamin D (1,25-dihydroxyvitamin D3) receptor	4187	4072G>A	3
J03490	J03490	246900	GEN-C5	Dihydrolipoamide dehydrogenase (E3 component of pyruvate dehydrogenase complex, 2-oxo-glutarate complex, branched chain keto acid dehydrogenase complex)	1569	1493A>C	N498T
J03490	J03490	246900	GEN-C5	Dihydrolipoamide dehydrogenase (E3 component of pyruvate dehydrogenase complex, 2-oxo-glutarate complex, branched chain keto acid dehydrogenase complex)	1624	1548T>A	3
J03490	J03490	246900	GEN-C5	Dihydrolipoamide dehydrogenase (E3 component of pyruvate dehydrogenase complex, 2-oxo-glutarate complex, branched chain keto acid dehydrogenase complex)	1813	1737A>G	3

J03490	J03490	246900	GEN-C5	branched chain keto acid dehydrogenase complex) Dihydrolipoamide dehydrogenase (E3 component of pyruvate dehydrogenase complex, 2-oxo-glutarate complex, branched chain keto acid dehydrogenase complex)	2096	2020T>C	3
J03548	J03548	103260	GEN-11M	Human adrenodoxin mRNA, complete cds	1099	967G>A	3
J03548	J03548	103260	GEN-11M	Human adrenodoxin mRNA, complete cds	1123	991T>C	3
J03548	J03548	103260	GEN-11M	Human adrenodoxin mRNA, complete cds	1222	1090G>C	3
J03548	J03548	103260	GEN-11M	Human adrenodoxin mRNA, complete cds	1254	1122G>A	3
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	501	479A>G	N160S
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	604	582C>T	S
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	803	781G>T	A261S
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	1042	1020C>T	S
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	1535	1513-1515CCT>CC	S
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	1535	1513- [P505V;50 1515delCCT 6-505del]	T
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	1797	1775A>G	D592G
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	2215	2193G>A	S
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	2350	2328A>G	S
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	2505	2483T>C	M828T
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	3409	3387T>C	S
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	3409	3387T>C	S

J05070	J05070	120361	GEN-16U	enzyme (ACE) Human type IV collagenase mRNA, complete cds	1840	1821A>C	S
J05070	J05070	120361	GEN-16U	Human type IV collagenase mRNA, complete cds	2101	2082G>A	S
J05070	J05070	120361	GEN-16U	Human type IV collagenase mRNA, complete cds	2146	2127C>T	3
J05070	J05070	120361	GEN-16U	Human type IV collagenase mRNA, complete cds	2288	2269T>C	3
J05158	J05158	603104	GEN-173	Human type IV collagenase mRNA, complete cds	2314	2314C>T	3
J05158	J05158	603104	GEN-173	Human carboxypeptidase N mRNA, 3 end	2316	2316G>T	3
J05158	J05158	603104	GEN-173	Human carboxypeptidase N mRNA, 3 end	2332	2332G>T	3
J05158	J05158	603104	GEN-173	Human carboxypeptidase N mRNA, 3 end	2541	2541G>A	3
J05158	J05158	603104	GEN-173	Human carboxypeptidase N mRNA, 3 end	2651	2651C>T	3
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	112	52G>A	A18T
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	121	61G>A	E21K
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	151	91G>A	E31K
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	197	137T>C	L46P
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	204	144delG	F
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	238	178A>G	T60A

K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	365	305C>G	P102R
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	409	349G>A	A117T
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	448	388T>C	C130R
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	494	434G>A	G145D
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	515	455G>A	R152Q
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	520	460C>A	R154S
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	538	478C>T	R160C
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	547	487C>T	R163C
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	548	488G>A	R163H
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	550	490A>G	K164E
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	586	526C>T	R176C
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	586	526C>T	R176C
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	743	683G>A	F
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	785	725G>A	R242Q

K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	796	736C>T	R246C
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	821	761T>A	V254E
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	865	805C>G	R269G
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	935	875G>A	R292H
K00396	K00396	107741	GEN-P0	Human apolipoprotein E (epsilon 2 and 3 alleles) mRNA	1000	940A>C	S314R
K01911	K01911	162640	GEN-2O	Neuropeptide Y mRNA	236	150G>A	S
K01911	K01911	162640	GEN-2O	Neuropeptide Y mRNA	290	204C>T	S
K02770	K02770	147720	GEN-5M	Interleukin 1, beta mRNA	19	(-68)A>C	5
K02770	K02770	147720	GEN-5M	Interleukin 1, beta mRNA	26	(-61)A>C	5
K02770	K02770	147720	GEN-5M	Interleukin 1, beta mRNA	48	(-39)C>T	5
K02770	K02770	147720	GEN-5M	Interleukin 1, beta mRNA	114	28G>A	E10K
K02770	K02770	147720	GEN-5M	Interleukin 1, beta mRNA	119	33G>A	M11I
K03195	K03195	138140	GEN-ZT	Human (HepG2) glucose transporter gene mRNA, complete cds	1484	1305C>T	S
K03195	K03195	138140	GEN-ZT	Human (HepG2) glucose transporter gene mRNA, complete cds	2120	1941G>C	3
KDR	X61656	191306	GEN-3BZ	H.sapiens mRNA for growth factor receptor tyrosine kinase	2308	2308A>G	T770A
KDR	X61656	191306	GEN-3BZ	H.sapiens mRNA for growth factor receptor tyrosine kinase	2353	2353G>C	G785R
KDR	X61656	191306	GEN-3BZ	H.sapiens mRNA for growth factor receptor tyrosine kinase	2499	2499C>G	N833K
KDR	X61656	191306	GEN-3BZ	H.sapiens mRNA for growth factor receptor tyrosine kinase	2537	2537A>T	E846V

KDR	X61656	191306	GEN-3BZ	tyrosine kinase H. sapiens mRNA for growth factor receptor	4123	4123G>C	3
L00352	L00352	143890	GEN-2S8	tyrosine kinase Human low density lipoprotein receptor gene, exon 18	71	72C>T	3
L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	103	104G>A	3
L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	716	717C>T	3
L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	881	882G>A	3
L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	1180	1181A>G	3
L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	1186	1187C>G	3
L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	1187	1188T>G	3
L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	1191	1192G>A	3
L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	1222	1223G>A	3
L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	1223	1224C>T	3
L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	1224	1225G>A	3
L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	1227	1228T>C	3
L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	1234	1235T>C	3

L00352	L00352	143890	2S8	lipoprotein receptor gene, exon 18	1252	1253A>T	3
L00352	GEN-2S8			Human low density lipoprotein receptor gene, exon 18			
L00352	L00352	143890	2S8	lipoprotein receptor gene, exon 18	1268	1269A>C	3
L00352	GEN-2S8			Human low density lipoprotein receptor gene, exon 18			
L00352	L00352	143890	2S8	lipoprotein receptor gene, exon 18	1268	1269A>T	3
L00352	GEN-2S8			Human low density lipoprotein receptor gene, exon 18			
L00352	L00352	143890	2S8	lipoprotein receptor gene, exon 18	1279	1280C>T	3
L00352	GEN-2S8			Human low density lipoprotein receptor gene, exon 18			
L00352	L00352	143890	2S8	lipoprotein receptor gene, exon 18	1280	1281G>A	3
L00352	GEN-2S8			Human low density lipoprotein receptor gene, exon 18			
L00352	L00352	143890	2S8	lipoprotein receptor gene, exon 18	1308	1309C>T	3
L00352	GEN-2S8			Human low density lipoprotein receptor gene, exon 18			
L00352	L00352	143890	2S8	lipoprotein receptor gene, exon 18	1309	1310G>A	3
L00352	GEN-2S8			Human low density lipoprotein receptor gene, exon 18			
L00352	L00352	143890	2S8	lipoprotein receptor gene, exon 18	1316	1317G>A	3
L00352	GEN-2S8			Human low density lipoprotein receptor gene, exon 18			
L00352	L00352	143890	2S8	lipoprotein receptor gene, exon 18	1320	1321T>C	3
L00352	GEN-2S8			Human low density lipoprotein receptor gene, exon 18			
L00352	L00352	143890	2S8	lipoprotein receptor gene, exon 18	1345	1346G>A	3
L00352	GEN-2S8			Human low density lipoprotein receptor gene, exon 18			
L00352	L00352	143890	2S8	lipoprotein receptor gene, exon 18	1368	1369T>C	3
L00352	GEN-2S8			Human low density lipoprotein receptor gene, exon 18			
L00352	L00352	143890	2S8	lipoprotein receptor gene, exon 18	1376	1377C>T	3
L00352	GEN-2S8			Human low density lipoprotein receptor gene, exon 18			
L00352	L00352	143890	2S8	lipoprotein receptor gene, exon 18	1383	1384C>T	3
L00352	GEN-2S8			Human low density lipoprotein receptor gene, exon 18			

L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	1406	1407T>C	3
L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	1418	1419G>C	3
L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	1428	1429T>C	3
L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	1453	1454C>T	3
L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	1796	1797T>C	3
L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	2108	2109G>A	3
L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	2490	2491A>C	3
L02932	L02932	170998	GEN-KW4	Human peroxisome proliferator activated receptor mRNA, complete cds	648	432G>A	S
L07592	L07592	600409	GEN-1E7	Human peroxisome proliferator activated receptor mRNA, complete cds	3119	2782C>G	3
L13286	L13286	600125	GEN-1O3	Human mitochondrial 1,25-dihydroxyvitamin D3 24-hydroxylase mRNA, complete cds	2031	1638G>A	3
L13436	L13436	108961	GEN-2Q	guanylate cyclase	1410	1411T>A	3
L13436	L13436	108961	GEN-2Q	guanylate cyclase	1646	1647C>G	3
L13436	L13436	108961	GEN-2Q	guanylate cyclase	1650	1651G>C	3
L13436	L13436	108961	GEN-2Q	guanylate cyclase	1677	1678C>G	3
L13436	L13436	108961	GEN-2Q	guanylate cyclase	2222	2223C>T	3
L13436	L13436	108961	GEN-2Q	guanylate cyclase	2444	2445C>T	3
L13858	L13858	182530	GEN-	Human guanine nucleotide	423	423T>C	S

L13858	L13858	182530	GEN-1PL	exchange factor mRNA, complete cds	3957	3957G>A	S
L17075	L17075	601284	GEN-1ZQ	Human guanine nucleotide exchange factor mRNA, complete cds	838	747G>A	S
L19182	L19182	602867	GEN-21Z	Human TGF- β superfamily receptor type I mRNA, complete cds	297	284G>A	R95K
L20859	L20859	137570	GEN-23V	Human MAC25 mRNA, complete cds	3141	2771A>G	3
L26232	L26232	172425	GEN-2AK	Human leukemia virus receptor 1 (GLVR1) mRNA, complete cds	906	819C>T	S
L26232	L26232	172425	GEN-2AK	Human phospholipid transfer protein mRNA, complete cds	1547	1460C>A	T487K
L27080	L27080	None	GEN-4G2	Human melanocortin 5 receptor (MC5R) gene, complete cds	146	(-38)A>C	5
L27080	L27080	None	GEN-4G2	Human melanocortin 5 receptor (MC5R) gene, complete cds	927	744C>T	S
L40992	L40992	600211	GEN-2SO	Homo sapiens (clone PEBP2aA1) core-binding factor, runt domain, alpha subunit 1 (CBFA1) mRNA, 3' end of cds	265	265G>A	V89I
L78207	L78207	600509	GEN-5Q	Cell surface receptor for sulfonyleureas on pancreatic b cells	4019	3981A>G	S
LEPR	U43168	601007	GEN-2UN	Human leptin receptor (Ob-r) mRNA, complete cds	446	253A>G	T85A
LEPR	U43168	601007	GEN-2UN	Human leptin receptor (Ob-r) mRNA, complete cds	519	326A>G	K109R
LEPR	U43168	601007	GEN-2UN	Human leptin receptor (Ob-r) mRNA, complete cds	861	668A>G	Q223R
LEPR	U43168	601007	GEN-2UN	Human leptin receptor (Ob-r) mRNA, complete cds	1222	1029T>C	S

LEPR	U43168	601007	GEN-2UN	Human leptin receptor (Ob-r) mRNA, complete cds	2161	1968G>C	K656N
LEPR	U43168	601007	GEN-2UN	Human leptin receptor (Ob-r) mRNA, complete cds	2174	1981A>C	T661P
LEPR	U43168	601007	GEN-2UN	Human leptin receptor (Ob-r) mRNA, complete cds	2764	2571T>G	S
LEPR	U43168	601007	GEN-2UN	Human leptin receptor (Ob-r) mRNA, complete cds	3151	2958C>T	S
LEPR	U43168	601007	GEN-2UN	Human leptin receptor (Ob-r) mRNA, complete cds	3250	3057G>A	S
LIPA	X76488	278000	GEN-3P2	H.sapiens mRNA for lysosomal acid lipase	191	46A>C	T16P
LIPA	X76488	278000	GEN-3P2	H.sapiens mRNA for lysosomal acid lipase	212	67G>A	G23R
LIPA	X76488	278000	GEN-3P2	H.sapiens mRNA for lysosomal acid lipase	967	822G>A	M274I
LIPA	X76488	278000	GEN-3P2	H.sapiens mRNA for lysosomal acid lipase	1531	1386C>T	3
LIPA	X76488	278000	GEN-3P2	H.sapiens mRNA for lysosomal acid lipase	2254	2109A>T	3
LIPA	X76488	278000	GEN-3P2	H.sapiens mRNA for lysosomal acid lipase	2439	2294C>T	3
LIPC	J03540	151670	GEN-11J	Human hepatic lipase mRNA, complete cds	469	465T>G	S
LIPC	J03540	151670	GEN-11J	Human hepatic lipase mRNA, complete cds	595	591A>G	S
LIPC	J03540	151670	GEN-11J	Human hepatic lipase mRNA, complete cds	648	644G>A	S215N
LIPC	J03540	151670	GEN-11J	Human hepatic lipase mRNA, complete cds	817	813C>T	S
LIPC	J03540	151670	GEN-11J	Human hepatic lipase mRNA, complete cds	1441	1437C>A	S
LRP1	D90070	107770	GEN-466	Human ATL-derived PMA-responsive (APR) peptide mRNA	686	513T>G	3
LRPAP1	M63959	104225	GEN-3EI	Human alpha-2-macroglobulin receptor-associated protein mRNA, complete cds	850	837G>A	S
LRPAP1	M63959	104225	GEN-3EI	Human alpha-2-macroglobulin receptor-associated protein mRNA, complete cds	1093	1080C>T	3

LRPAP1	M63959	104225	GEN-3EI	associated protein mRNA, complete cds	1175	1162G>A	3
				Human alpha-2- macroglobulin receptor- associated protein mRNA, complete cds			
LRPAP1	M63959	104225	GEN-3EI	Human alpha-2- macroglobulin receptor- associated protein mRNA, complete cds	1249	1236C>T	3
				Human alpha-2- macroglobulin receptor- associated protein mRNA, complete cds			
LRPAP1	M63959	104225	GEN-3EI	Human alpha-2- macroglobulin receptor- associated protein mRNA, complete cds	1249	1236C>T	3
				Human alpha-2- macroglobulin receptor- associated protein mRNA, complete cds			
LRPAP1	M63959	104225	GEN-3EI	Human alpha-2- macroglobulin receptor- associated protein mRNA, complete cds	1392	1379T>G	3
				Human alpha-2- macroglobulin receptor- associated protein mRNA, complete cds			
M10051	M10051	147670	GEN-2V	Insulin receptor	2757	2619G>A	S
M10051	M10051	147670	GEN-2V	Insulin receptor	4391	4253G>A	3
M10901	M10901	138040	GEN-2W	Corticosteroid nuclear receptor b	1220	1088A>G	N363S
M10901	M10901	138040	GEN-2W	Corticosteroid nuclear receptor b	2024	1892- 1893AG>AG	S
M10901	M10901	138040	GEN-2W	Corticosteroid nuclear receptor b	2024	1892- 1893delAG	F
M10901	M10901	138040	GEN-2W	Corticosteroid nuclear receptor b	2054	1922A>T	D641V
M10901	M10901	138040	GEN-2W	Corticosteroid nuclear receptor b	2372	2240T>G	I747S
M10901	M10901	138040	GEN-2W	Corticosteroid nuclear receptor b	2391	2259A>C	L753F
M10901	M10901	138040	GEN-2W	Corticosteroid nuclear receptor b	2391	2259A>T	L753F
M11050	M11050	138040	GEN-7Y	Glucocorticoid receptor	2166	2034C>T	S
M11050	M11050	138040	GEN-7Y	Glucocorticoid receptor	3353	3221T>G	3
M11050	M11050	138040	GEN-7Y	Glucocorticoid receptor	3398	3266T>G	3
M11717	M11717	140550	GEN- MF3	Human heat shock protein (hsp 70) gene, complete cds	54	(-162)G>A	5

M11717	M11717	140550	GEN-MF3	Human heat shock protein (hsp 70) gene, complete cds	190	(-26)C>G	5
M11717	M11717	140550	GEN-MF3	Human heat shock protein (hsp 70) gene, complete cds	320	105C>T	S
M11717	M11717	140550	GEN-MF3	Human heat shock protein (hsp 70) gene, complete cds	390	175G>A	V59M
M11717	M11717	140550	GEN-MF3	Human heat shock protein (hsp 70) gene, complete cds	431	216C>G	S
M11717	M11717	140550	GEN-MF3	Human heat shock protein (hsp 70) gene, complete cds	545	330G>C	E110D
M11717	M11717	140550	GEN-MF3	Human heat shock protein (hsp 70) gene, complete cds	1907	1692C>G	S
M11717	M11717	140550	GEN-MF3	Human heat shock protein (hsp 70) gene, complete cds	2319	2104A>G	3
M12578	M12578	152760	GEN-2Y	Gonadotropin-releasing hormone (leutinizing-releasing hormone)	79	47G>C	W16S
M12674	M12674	133430	GEN-7Z	Estrogen receptor	1267	975C>G	S
M13509	M13509	120353	GEN-QJ	Human skin collagenase mRNA, complete cds	383	315A>G	S
M13509	M13509	120353	GEN-QJ	Human skin collagenase mRNA, complete cds	899	831G>A	S
M13509	M13509	120353	GEN-QJ	Human skin collagenase mRNA, complete cds	1522	1454A>G	3
M13509	M13509	120353	GEN-QJ	Human skin collagenase mRNA, complete cds	1747	1679C>T	3
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	184	(-11)T>C	5
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	270	76G>C	V26L
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	446	252C>T	S

M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1254	1060C>G	3
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1306	1112G>A	3
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1336	1142T>A	3
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1338	1144C>T	3
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1451	1257G>A	3
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1462	1268C>T	3
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1522	1328G>C	3
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1557	1363G>C	3
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1585	1391C>A	3
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1630	1436T>C	3
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1668	1474T>G	3
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1712	1518C>G	3
M14221	M14221	161565	GEN-QM	Human cathepsin B proteinase mRNA, complete cds	1898	1704A>G	3
M14565	M14565	118485	GEN-30	Cytochrome P450, complete cds	947	903G>C	M301I

SD-144146.1

M15856	M15856	238600	GEN-33	Lipoprotein lipase	836	662T>C	I221T
M15856	M15856	238600	GEN-33	Lipoprotein lipase	839	665G>A	G222E
M15856	M15856	238600	GEN-33	Lipoprotein lipase	843	669C>T	S
M15856	M15856	238600	GEN-33	Lipoprotein lipase	867	693C>G	D231E
M15856	M15856	238600	GEN-33	Lipoprotein lipase	875	701C>T	P234L
M15856	M15856	238600	GEN-33	Lipoprotein lipase	916	742delG	F
M15856	M15856	238600	GEN-33	Lipoprotein lipase	983	809G>A	R270H
M15856	M15856	238600	GEN-33	Lipoprotein lipase	985	811T>A	S271T
M15856	M15856	238600	GEN-33	Lipoprotein lipase	1003	829G>A	D277N
M15856	M15856	238600	GEN-33	Lipoprotein lipase	1127	953A>G	N318S
M15856	M15856	238600	GEN-33	Lipoprotein lipase	1255	1081G>A	A361T
M15856	M15856	238600	GEN-33	Lipoprotein lipase	1348	1174C>G	L392V
M15856	M15856	238600	GEN-33	Lipoprotein lipase	1401	1227G>A	F
M15856	M15856	238600	GEN-33	Lipoprotein lipase	1508	1334G>A	C445Y
M15856	M15856	238600	GEN-33	Lipoprotein lipase	1553	1379C>T	A460V
M15856	M15856	238600	GEN-33	Lipoprotein lipase	1595	1421C>G	F
M15856	M15856	238600	GEN-33	Lipoprotein lipase	1611	1437G>A	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	1973	1799T>C	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	2428	2254T>A	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	2743	2569T>C	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	2851	2677A>G	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	2851	2677A>G	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	2958	2784G>A	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	3017	2843T>C	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	3272	3098T>C	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	3272	3098T>C	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	3343	3169T>C	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	3447	3273C>T	3
M16660	M16660	140571	GEN-1YC	Human 90-kDa heat-shock protein gene, cDNA, complete cds	825	741G>A	S
M16660	M16660	140571	GEN-1YC	Human 90-kDa heat-shock protein gene, cDNA, complete cds	825	741G>A	S
M16801	M16801	600983	GEN-36	Mineralocorticoid receptor (aldosterone receptor)	175	(-42)C>G	5
M16801	M16801	600983	GEN-36	Mineralocorticoid receptor	754	538A>G	I180V

M16801	M16801	600983	GEN-36	(aldosterone receptor)	938	722C>T	A241V
				Mineralocorticoid receptor			
M16801	M16801	600983	GEN-36	(aldosterone receptor)	1221	1005delC	F
				Mineralocorticoid receptor			
M16801	M16801	600983	GEN-36	(aldosterone receptor)	1591	1375delT	F
				Mineralocorticoid receptor			
M16801	M16801	600983	GEN-36	(aldosterone receptor)	1713	1497C>T	S
				Mineralocorticoid receptor			
M16801	M16801	600983	GEN-36	(aldosterone receptor)	1825	1609C>T	F
				Mineralocorticoid receptor			
M16801	M16801	600983	GEN-36	(aldosterone receptor)	2438	2222T>G	V741G
				Mineralocorticoid receptor			
M16801	M16801	600983	GEN-36	(aldosterone receptor)	2730	2514G>A	S
				Mineralocorticoid receptor			
M16801	M16801	600983	GEN-36	(aldosterone receptor)	5243	5027T>A	3
				Mineralocorticoid receptor			
M16801	M16801	600983	GEN-36	(aldosterone receptor)	5645	5429G>A	3
				Mineralocorticoid receptor			
M16827	M16827	201450	GEN-EI	(aldosterone receptor)	1956	1938T>C	3
				Acyl-Coenzyme A			
				dehydrogenase, C-4 to C-12 straight chain			
M20132	M20132	313700	GEN-38	Androgen receptor	995	633G>A	S
				(dihydrotestosterone receptor)			
M20132	M20132	313700	GEN-38	Androgen receptor	1385	1023T>C	S
				(dihydrotestosterone receptor)			
M20132	M20132	313700	GEN-38	Androgen receptor	1786	1424G>A	G475E
				(dihydrotestosterone receptor)			
M20566	M20566	147880	GEN-3A	Interleukin 6A	3058	2621A>T	3
M20681	M20681	138170	GEN-230	Human glucose transporter-like protein-III (GLUT3), complete cds	1550	1308C>T	S
				Human glucose transporter-like protein-III (GLUT3), complete cds			
M20681	M20681	138170	GEN-230	Human glucose transporter-like protein-III (GLUT3), complete cds	3179	2937T>C	3
				Human glucose transporter-like protein-III (GLUT3), complete cds			
M20681	M20681	138170	GEN-230	Human glucose transporter-like protein-III (GLUT3), complete cds	3238	2996C>T	3
				Human glucose transporter-like protein-III (GLUT3), complete cds			

M20681	M20681	138170	GEN-230	Human glucose transporter-like protein-III (GLUT3), complete cds	3356	3114T>C	3
M20681	M20681	138170	GEN-230	Human glucose transporter-like protein-III (GLUT3), complete cds	3378	3136T>C	3
M20681	M20681	138170	GEN-230	Human glucose transporter-like protein-III (GLUT3), complete cds	3524	3282C>A	3
M20681	M20681	138170	GEN-230	Human glucose transporter-like protein-III (GLUT3), complete cds	3572	3330G>T	3
M23725	M23725	179050	GEN-ES	Pyruvate kinase, muscle	547	438C>T	S
M23725	M23725	179050	GEN-ES	Pyruvate kinase, muscle	850	741G>A	S
M23725	M23725	179050	GEN-ES	Pyruvate kinase, muscle	1259	1150G>A	E384K
M24857	M24857	180190	GEN-80	Retinoic acid receptor, gamma 1	1694	1280C>T	S427L
M26393	M26393	201470	GEN-EW	Acyl-Coenzyme A dehydrogenase, C-2 to C-3 short chain	1797	1765A>G	3
M27137	M27137	109715	GEN-5W	3beta hydroxysteroid dehydrogenase	1103	1100C>A	T367N
M27492	M27492	147810	GEN-3F	INTERLEUKIN 1 RECEPTOR, TYPE I	4686	4604T>G	3
M27875	M27875	107680	GEN-2CK	Human apolipoprotein A-I mRNA, complete cds	34	15G>C	S
M27875	M27875	107680	GEN-2CK	Human apolipoprotein A-I mRNA, complete cds	202	183C>T	S
M27875	M27875	107680	GEN-2CK	Human apolipoprotein A-I mRNA, complete cds	204	185T>G	L62W
M27875	M27875	107680	GEN-2CK	Human apolipoprotein A-I mRNA, complete cds	255	236C>T	S79F
M27875	M27875	107680	GEN-2CK	Human apolipoprotein A-I mRNA, complete cds	689	670C>T	S
M27875	M27875	107680	GEN-2CK	Human apolipoprotein A-I mRNA, complete cds	824	805G>A	3
M28614	M28614	107720	GEN-6Q	Apolipoprotein C-III	370	340C>G	3
M28614	M28614	107720	GEN-6Q	Apolipoprotein C-III	401	371T>G	3
M28614	M28614	107720	GEN-6Q	Apolipoprotein C-III	479	449T>A	3

M29882	M29882	107670	GEN-6R	Apolipoprotein A-II	26	17C>A	A6E
M29882	M29882	107670	GEN-6R	Apolipoprotein A-II	183	174G>A	S
M29882	M29882	107670	GEN-6R	Apolipoprotein A-II	192	183C>A	S
M30262	M30262	600295	GEN-WA	Human cardiolipin-atrial natriuretic factor (CDD- ANF) mRNA, complete cds	178	79C>T	P27S
M30262	M30262	600295	GEN-WA	Human cardiolipin-atrial natriuretic factor (CDD- ANF) mRNA, complete cds	178	79C>T	P27S
M30262	M30262	600295	GEN-WA	Human cardiolipin-atrial natriuretic factor (CDD- ANF) mRNA, complete cds	203	104C>G	A35G
M30262	M30262	600295	GEN-WA	Human cardiolipin-atrial natriuretic factor (CDD- ANF) mRNA, complete cds	203	104C>G	A35G
M30262	M30262	600295	GEN-WA	Human cardiolipin-atrial natriuretic factor (CDD- ANF) mRNA, complete cds	210	111G>T	S
M30262	M30262	600295	GEN-WA	Human cardiolipin-atrial natriuretic factor (CDD- ANF) mRNA, complete cds	210	111G>T	S
M30262	M30262	600295	GEN-WA	Human cardiolipin-atrial natriuretic factor (CDD- ANF) mRNA, complete cds	327	228C>T	S
M30262	M30262	600295	GEN-WA	Human cardiolipin-atrial natriuretic factor (CDD- ANF) mRNA, complete cds	327	228C>T	S
M30262	M30262	600295	GEN-WA	Human cardiolipin-atrial natriuretic factor (CDD- ANF) mRNA, complete cds	553	454T>C	F
M30262	M30262	600295	GEN-WA	Human cardiolipin-atrial natriuretic factor (CDD- ANF) mRNA, complete cds	553	454T>C	F
M30262	M30262	600295	GEN-WA	Human cardiolipin-atrial natriuretic factor (CDD- ANF) mRNA, complete cds	626	527G>T	3
M30262	M30262	600295	GEN-WA	Human cardiolipin-atrial natriuretic factor (CDD- ANF) mRNA, complete cds	626	527G>T	3
M30262	M30262	600295	GEN-WA	Human cardiolipin-atrial natriuretic factor (CDD- ANF) mRNA, complete cds	640	541T>C	3

M30262	M30262	600295	GEN-WA	ANF) mRNA, complete cds	640	541T>C	3
				Human cardiolipin-atrial natriuretic factor (CDD-ANF) mRNA, complete cds			
M31145	M31145	146730	GEN-3J	Insulin-like growth factor binding protein 1 precursor	923	759A>G	1253M
M31145	M31145	146730	GEN-3J	Insulin-like growth factor binding protein 1 precursor	1048	884T>C	3
M31145	M31145	146730	GEN-3J	Insulin-like growth factor binding protein 1 precursor	1260	1096C>G	3
M31159	M31159	146732	GEN-2GD	Human growth hormone-dependent insulin-like growth factor-binding protein mRNA, complete cds	204	95G>C	G32A
M31159	M31159	146732	GEN-2GD	Human growth hormone-dependent insulin-like growth factor-binding protein mRNA, complete cds	2178	2069A>T	3
M31328	M31328	139130	GEN-7G	Guanine nucleotide binding protein (G protein), beta polypeptide 3	1049	1043G>A	3
M32313	M32313	184753	GEN-5Y	Steroid 5 alpha reductase 1	1271	1241C>T	3
M32313	M32313	184753	GEN-5Y	Steroid 5 alpha reductase 1	1344	1314G>A	3
M32313	M32313	184753	GEN-5Y	Steroid 5 alpha reductase 1	1489	1459G>A	3
M32313	M32313	184753	GEN-5Y	Steroid 5 alpha reductase 1	1780	1750T>C	3
M34479	M34479	179060	GEN-F9	Pyruvate dehydrogenase (lipoamide) beta	109	109G>A	D37N
M34479	M34479	179060	GEN-F9	Pyruvate dehydrogenase (lipoamide) beta	438	438A>G	S
M34479	M34479	179060	GEN-F9	Pyruvate dehydrogenase (lipoamide) beta	1172	1172A>C	3
M34479	M34479	179060	GEN-F9	Pyruvate dehydrogenase (lipoamide) beta	1179	1179C>T	3
M34479	M34479	179060	GEN-F9	Pyruvate dehydrogenase (lipoamide) beta	1323	1323C>A	3

M34479	M34479	179060	GEN-F9	Pyruvate dehydrogenase (lipoamide) beta	1376	1376G>C	3
M34479	M34479	179060	GEN-F9	Pyruvate dehydrogenase (lipoamide) beta	1433	1433C>T	3
M34720	M34720	103880	GEN-RH	aldose reductase	676	663C>A	S
M34720	M34720	103880	GEN-RH	aldose reductase	1176	1163C>A	3
M37825	M37825	165190	GEN-20M	Human fibroblast growth factor-5 (FGF-5) mRNA, complete cds	787	648T>G	S
M54968	M54968	190070	GEN-35G	Human K-ras oncogene protein mRNA, complete cds	711	519T>C	S
M54968	M54968	190070	GEN-35G	Human K-ras oncogene protein mRNA, complete cds	936	744G>T	3
M54968	M54968	190070	GEN-35G	Human K-ras oncogene protein mRNA, complete cds	1270	1078T>C	3
M54968	M54968	190070	GEN-35G	Human K-ras oncogene protein mRNA, complete cds	3268	3076T>G	3
M54968	M54968	190070	GEN-35G	Human K-ras oncogene protein mRNA, complete cds	4529	4337A>C	3
M54968	M54968	190070	GEN-35G	Human K-ras oncogene protein mRNA, complete cds	4555	4363A>G	3
M54968	M54968	190070	GEN-35G	Human K-ras oncogene protein mRNA, complete cds	4672	4480A>C	3
M55531	M55531	138230	GEN-FF	Solute carrier family 2 (facilitated glucose transporter), member 5	1208	1133T>G	V378G
M55531	M55531	138230	GEN-FF	Solute carrier family 2 (facilitated glucose transporter), member 5	1975	1900C>T	3
M55531	M55531	138230	GEN-FF	Solute carrier family 2 (facilitated glucose transporter), member 5	1985	1910A>G	3
M57899	M57899	191740	GEN-38A	Solute carrier family 2 (facilitated glucose transporter), member 5 Human bilirubin UDP-glucuronosyltransferase	1828	1813C>T	3

M57899	M57899	191740	GEN-38A	isozyme 1 mRNA, complete cds Human bilirubin UDP-glucuronosyltransferase isozyme 1 mRNA, complete cds	1956	1941C>G	3
M57899	M57899	191740	GEN-38A	Human bilirubin UDP-glucuronosyltransferase isozyme 1 mRNA, complete cds	2057	2042C>G	3
M59305	M59305	108962	GEN-39P	Human atrial natriuretic peptide clearance receptor (ANP C-receptor) mRNA, complete cds	160	(-203)-(-199)delTTTTT	F
M59830	M59830	603012	GEN-MSB	Human MHC class III HSP70-2 gene (HLA), complete cds	1860	1860C>G	S
M61906	M61906	171833	GEN-RV	Human P13-kinase associated p85 mRNA sequence	3112	3113A>G	3
M62782	M62782	146734	GEN-3CU	Homo sapiens insulin-like growth factor binding protein 5 (IGFBP-5) mRNA, complete cds	908	852C>T	3
M63960	M63960	176875	GEN-FT	Protein phosphatase 1, catalytic subunit, alpha isoform	1087	1058G>T	3
M63960	M63960	176875	GEN-FT	Protein phosphatase 1, catalytic subunit, alpha isoform	1292	1263G>A	3
M64590	M64590	238300	GEN-FU	Glycine cleavage system: Protein P	3076	2926A>G	M976V
M64710	M64710	None	GEN-KUW	Human C-type natriuretic peptide gene, complete cds	199	200C>G	3
M64710	M64710	None	GEN-KUW	Human C-type natriuretic peptide gene, complete cds	777	778G>A	3
M64710	M64710	None	GEN-KUW	Human C-type natriuretic peptide gene, complete cds	1215	1216A>G	3

M65028	M65028	602372	GEN-3FM	Human hnRNP type A/B protein mRNA, complete cds	273	131C>G	P44R
M65028	M65028	602372	GEN-3FM	Human hnRNP type A/B protein mRNA, complete cds	595	453C>G	S
M65028	M65028	602372	GEN-3FM	Human hnRNP type A/B protein mRNA, complete cds	1255	1113A>G	3
M68867	M68867	180231	GEN-S1	Human cellular retinoic acid-binding protein II (CRABP) mRNA, complete cds	604	506C>A	3
M82962	M82962	600388	GEN-3XC	Human N-benzoyl-L-tyrosyl-p-amino-benzoic acid hydrolase alpha subunit (PPH alpha) mRNA, complete cds	2316	2307T>G	3
M82962	M82962	600388	GEN-3XC	Human N-benzoyl-L-tyrosyl-p-amino-benzoic acid hydrolase alpha subunit (PPH alpha) mRNA, complete cds	2428	2419A>C	3
M83667	M83667	116898	GEN-3YG	Human NF-IL6-beta protein mRNA, complete cds	574	486G>T	E162D
M83667	M83667	116898	GEN-3YG	Human NF-IL6-beta protein mRNA, complete cds	578	490C>T	P164S
M83667	M83667	116898	GEN-3YG	Human NF-IL6-beta protein mRNA, complete cds	581	493C>T	R165C
M83667	M83667	116898	GEN-3YG	Human NF-IL6-beta protein mRNA, complete cds	974	886C>G	3
M84755	M84755	162641	GEN-46	Neuropeptide Y1	1121	1121A>C	K374T
M86553	M86553	116845	GEN-416	Human cathepsin S mRNA, complete cds	26	20T>C	V7A
M86553	M86553	116845	GEN-416	Human cathepsin S mRNA, complete cds	487	481A>T	T161S
M86553	M86553	116845	GEN-416	Human cathepsin S mRNA, complete cds	705	699G>C	S

M86553	M86553	116845	GEN-416	mRNA, complete cds	1149	1143T>G	3
				Human cathepsin S			
M87290	M87290	106165	GEN-19	mRNA, complete cds	296	16T>C	S6P
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	413	133G>A	G45R
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	853	573T>C	S
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	853	573T>C	S
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	1342	1062A>G	S
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	1342	1062A>G	S
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	1430	1150T>G	3
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	1446	1166C>A	3
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	1446	1166C>A	3
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	1446	1166C>A	3
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	1453	1173A>G	3
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	1677	1397G>A	3
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	1797	1517G>T	3
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	1885	1605C>T	3
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	1916	1636T>C	3
M87290	M87290	106165	GEN-19	Angiotensin receptor AT1	2158	1878A>G	3
M90516	M90516	138292	GEN-GI	Glutamine-fructose-6-phosphate transaminase	2968	2846T>G	3
M93415	M93415	102581	GEN-48S	Human activin type II receptor mRNA, complete cds	136	(-38)G>T	5
MC1R	X67594	155555	GEN-4G4	H.sapiens mRNA for MSH receptor	346	178G>T	V60L
MC1R	X67594	155555	GEN-4G4	H.sapiens mRNA for MSH receptor	656	488A>G	Q163R
MC1R	X67594	155555	GEN-4G4	H.sapiens mRNA for MSH receptor	1068	900C>T	S
MC1R	X67594	155555	GEN-4G4	H.sapiens mRNA for MSH receptor	1110	942A>G	S
MC1R	X67594	155555	GEN-4G4	H.sapiens mRNA for MSH receptor	1134	966G>A	3
MET	M35074	164860	GEN-2LU	Human met oncogene mRNA, 3 end	60	60C>T	S
MET	M35074	164860	GEN-2LU	Human met oncogene mRNA, 3 end	294	294G>A	S

MGP	M58549	154870	GEN-38Y	Human matrix Gla protein (MGP) mRNA, complete cds	330	304A>G	T102A
MMP12	L23808	601046	GEN-27J	Human metalloproteinase (HME) mRNA, complete cds	1082	1070A>G	N357S
MMP2	D85510	602261	GEN-40A	Homo sapiens mRNA for MCP-2, partial cds	2389	2389G>C	3
MPV17	X76538	600945	GEN-3P6	H.sapiens Mpv17 mRNA	575	548C>T	3
MTP	X75500	157147	GEN-3O7	H.sapiens mRNA for microsomal triglyceride transfer protein	1847	1823T>G	F608C
MTP	X75500	157147	GEN-3O7	H.sapiens mRNA for microsomal triglyceride transfer protein	3231	3207G>A	3
NGFB	X52599	162030	GEN-33V	Human mRNA for beta nerve growth factor	832	663G>A	S
NGFR	M14764	162010	GEN-1S8	Human nerve growth factor receptor mRNA, complete cds	2716	2603C>T	3
NGFR	M14764	162010	GEN-1S8	Human nerve growth factor receptor mRNA, complete cds	2729	2616C>T	3
NGFR	M14764	162010	GEN-1S8	Human nerve growth factor receptor mRNA, complete cds	2912	2799G>A	3
NGFR	M14764	162010	GEN-1S8	Human nerve growth factor receptor mRNA, complete cds	3252	3139C>G	3
NOS1	U17327	163731	GEN-209	Human neuronal nitric oxide synthase (NOS1) mRNA, complete cds	3391	2706C>T	S
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	1380	1155C>T	S
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	1380	1155C>T	S
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	1503	1278C>T	S
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	1503	1278C>T	S

NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	2048	1823C>T	S608L
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	2048	1823C>T	S608L
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	2287	2062G>A	G688S
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	2287	2062G>A	G688S
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	2339	2114A>G	D705G
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	2339	2114A>G	D705G
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	2583	2358T>C	S
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	2583	2358T>C	S
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	2982	2757A>G	S
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	2982	2757A>G	S
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	3022	2797C>G	R933G
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	3022	2797C>G	R933G
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	3051	2826C>T	S
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	3051	2826C>T	S
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	3693	3468T>C	3
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	3693	3468T>C	3
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	3715	3490G>A	3
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	3715	3490G>A	3
NRAS	X02751	164790	GEN-XG	Human N-ras mRNA and flanking regions	221	(-506)A>G	5
NRAS	X02751	164790	GEN-XG	Human N-ras mRNA and flanking regions	390	(-337)C>A	5
NTRK1	X66397	191315	GEN-	H.sapiens tpr mRNA	2632	2335G>A	V779I

NTRK3	U05012	191316	3GN GEN- 16V	Human receptor tyrosine kinase TrkC (NTRK3) mRNA, complete cds	364	209G>A	S70N
NTRK3	U05012	191316	GEN- 16V	Human receptor tyrosine kinase TrkC (NTRK3) mRNA, complete cds	728	573C>T	S
NTRK3	U05012	191316	GEN- 16V	Human receptor tyrosine kinase TrkC (NTRK3) mRNA, complete cds	1613	1458C>T	S
NTRK3	U05012	191316	GEN- 16V	Human receptor tyrosine kinase TrkC (NTRK3) mRNA, complete cds	1643	1488G>C	S
OSBP	M86917	167040	GEN-425	Human oxysterol-binding protein (OSBP) mRNA, complete cds	216	(-265)T>G	5
OSBP	M86917	167040	GEN-425	Human oxysterol-binding protein (OSBP) mRNA, complete cds	802	322C>T	F
OSBP	M86917	167040	GEN-425	Human oxysterol-binding protein (OSBP) mRNA, complete cds	888	408C>T	S
OSBP	M86917	167040	GEN-425	Human oxysterol-binding protein (OSBP) mRNA, complete cds	934	454T>G	S152A
PACE	X17094	136950	GEN- 1ZV	Human fur mRNA for furin	399	183C>T	S
PACE	X17094	136950	GEN- 1ZV	Human fur mRNA for furin	1692	1476C>T	S
PACE	X17094	136950	GEN- 1ZV	Human fur mRNA for furin	2067	1851C>G	S
PACE	X17094	136950	GEN- 1ZV	Human fur mRNA for furin	2725	2509T>C	3
PACE	X17094	136950	GEN- 1ZV	Human fur mRNA for furin	2855	2639C>A	3
PACE	X17094	136950	GEN- 1ZV	Human fur mRNA for furin	2988	2772G>A	3
PACE	X17094	136950	GEN- 1ZV	Human fur mRNA for furin	3234	3018C>T	3
PACE	X17094	136950	GEN- 1ZV	Human fur mRNA for furin	3625	3409A>G	3

PACE	X17094	136950	GEN-1ZV	Human fur mRNA for furin	3883	3667C>T	3
PACE	X17094	136950	GEN-1ZV	Human fur mRNA for furin	4053	3837A>G	3
PAM	M37721	170270	GEN-2OK	Human peptidylglycine alpha-amidating monooxygenase mRNA, complete cds	3183	2995T>A	3
PAM	M37721	170270	GEN-2OK	Human peptidylglycine alpha-amidating monooxygenase mRNA, complete cds	3530	3342A>G	3
PAX6	M77844	106210	GEN-3QG	H.sapiens oculorhombin (aniridia) mRNA, complete cds	669	307C>T	F
PC	U04641	266150	GEN-150	Human pyruvate carboxylase (PC) mRNA, complete cds	1391	1353C>T	S
PC	U04641	266150	GEN-150	Human pyruvate carboxylase (PC) mRNA, complete cds	2219	2181C>T	S
PC	U04641	266150	GEN-150	Human pyruvate carboxylase (PC) mRNA, complete cds	2912	2874G>T	S
PC	U04641	266150	GEN-150	Human pyruvate carboxylase (PC) mRNA, complete cds	3897	3859C>T	3
PCK1	L05144	261680	GEN-172	Homo sapiens (clone lamda-hPEC-3) phosphoenolpyruvate carboxykinase (PCK1) mRNA, complete cds	1223	1102G>A	V368I
PDHA1	X52709	312170	GEN-33Y	Human mRNA for brain pyruvate dehydrogenase (EC 1.2.4.1)	849	795A>G	S
PDHA1	X52709	312170	GEN-33Y	Human mRNA for brain pyruvate dehydrogenase (EC 1.2.4.1)	1337	1283C>T	3
PDHA1	X52709	312170	GEN-33Y	Human mRNA for brain pyruvate dehydrogenase (EC 1.2.4.1)	1416	1362G>A	3

PEDF	M90439	172860	GEN-46E	Human molecular marker (EPC-1) gene, complete cds	40	2T>C	F
PEDF	M90439	172860	GEN-46E	Human molecular marker (EPC-1) gene, complete cds	215	177T>C	S
PEDF	M90439	172860	GEN-46E	Human molecular marker (EPC-1) gene, complete cds	788	750C>T	S
PEDF	M90439	172860	GEN-46E	Human molecular marker (EPC-1) gene, complete cds	900	862C>G	R288G
PEDF	M90439	172860	GEN-46E	Human molecular marker (EPC-1) gene, complete cds	952	914G>T	G305V
PHKG2	M31606	172471	GEN-2H7	Human phosphorylase kinase (PSK-C3) mRNA, complete cds	1155	1062C>G	S
PNLIP	M93285	246600	GEN-48N	Pancreatic lipase (PNLIP) (Dietary supplement)	646	646G>T	V216L
POMC	M28636	176830	GEN-2DG	Adrenocorticotrophic hormone (ACTH)	92	92C>T	3
PREP	X74496	600400	GEN-3N8	Prolyl Endopeptidase	390	390T>C	S
PREP	X74496	600400	GEN-3N8	Prolyl Endopeptidase	1051	1051T>G	L351V
PREP	X74496	600400	GEN-3N8	Prolyl Endopeptidase	1125	1125C>T	S
PREP	X74496	600400	GEN-3N8	Prolyl Endopeptidase	1363	1363G>A	V455M
PTHLH	J03580	168470	GEN-11U	Human, parathyroid-like protein (associated with humoral hypercalcemia of malignancy) mRNA, complete cds	975	37G>A	V13M
PTHLH	J03580	168470	GEN-11U	Human, parathyroid-like protein (associated with humoral hypercalcemia of malignancy) mRNA, complete cds	996	58G>A	V20M
PTPRF	Y00815	179590	GEN-UH	Human mRNA for LCA-	6939	6569A>G	3

PYGB	J03544	138550	GEN-11L	homolog. LAR protein (leukocyte antigen related) Human brain glycogen phosphorylase mRNA, complete cds	718	639C>T	S
PYGB	J03544	138550	GEN-11L	Human brain glycogen phosphorylase mRNA, complete cds	2449	2370G>A	S
PYGB	J03544	138550	GEN-11L	Human brain glycogen phosphorylase mRNA, complete cds	2712	2633C>G	3
PYGB	J03544	138550	GEN-11L	Human brain glycogen phosphorylase mRNA, complete cds	3346	3267C>T	3
PYGB	J03544	138550	GEN-11L	Human brain glycogen phosphorylase mRNA, complete cds	3644	3565G>A	3
PYGB	J03544	138550	GEN-11L	Human brain glycogen phosphorylase mRNA, complete cds	3687	3608G>A	3
PYGB	J03544	138550	GEN-11L	Human brain glycogen phosphorylase mRNA, complete cds	3770	3691G>A	3
PYGL	M36807	232700	GEN- 2NJ	Human liver glycogen phosphorylase type IV mRNA, 3 end	702	702G>C	R234S
PYGL	M36807	232700	GEN- 2NJ	Human liver glycogen phosphorylase type IV mRNA, 3 end	1108	1108C>G	3
RAF1	X06409	164760	GEN- 19K	Human mRNA fragment for activated c-raf-1 (exons 8- 17)	486	487T>C	3
RAF1	X06409	164760	GEN- 19K	Human mRNA fragment for activated c-raf-1 (exons 8- 17)	1947	1948C>T	3
RAF1	X06409	164760	GEN- 19K	Human mRNA fragment for activated c-raf-1 (exons 8- 17)	1992	1993C>A	3
S63912	S63912	601233	GEN- 3EJ	D10S102=FBRNP [human, fetal brain, mRNA, 3043 nt]	2193	2163G>A	3
S70154	S70154	100678	GEN-GY	ACAT2	669	632A>G	K211R

S70154	S70154	100678	GEN-GY	ACAT2	820	783T>C	S
S70154	S70154	100678	GEN-GY	ACAT2	820	783T>C	S
S70154	S70154	100678	GEN-GY	ACAT2	856	819G>A	S
S70154	S70154	100678	GEN-GY	ACAT2	856	819G>A	S
S70154	S70154	100678	GEN-GY	ACAT2	1388	1351T>G	3
S70154	S70154	100678	GEN-GY	ACAT2	1395	1358-1362CTTTA>	3
S70154	S70154	100678	GEN-GY	ACAT2	1395	CTTTA	F
S70154	S70154	100678	GEN-GY	ACAT2	1395	1358-1362delCTTT	
S70154	S70154	100678	GEN-GY	ACAT2	1419	A	3
S70154	S70154	100678	GEN-GY	ACAT2	1419	1382C>A	3
S74445	S74445	180230	GEN-3N7	cellular retinoic acid-binding protein [human, skin, mRNA, 735 nt]	134	60G>C	S
SLC5A1	M24847	182380	GEN-28S	Human Na ⁺ /glucose cotransporter 1 mRNA, complete cds	2226	2216C>T	3
SLO	U02632	600150	GEN-XA	Calcium-activated potassium channel	2377	2377T>G	S793A
SOD2	X07834	147460	GEN-1ES	Human mRNA for manganese superoxide dismutase (EC 1.15.1.1)	44	40C>G	P14A
SOD2	X07834	147460	GEN-1ES	Human mRNA for manganese superoxide dismutase (EC 1.15.1.1)	51	47T>C	V16A
SOD2	X07834	147460	GEN-1ES	Human mRNA for manganese superoxide dismutase (EC 1.15.1.1)	198	194C>A	T65N
SOD2	X07834	147460	GEN-1ES	Human mRNA for manganese superoxide dismutase (EC 1.15.1.1)	249	245T>C	I82T
SORD	U07361	182500	GEN-1DR	Homo sapiens sorbitol dehydrogenase gene, complete cds	606	465C>T	S
SORD	U07361	182500	GEN-1DR	Homo sapiens sorbitol dehydrogenase gene, complete cds	857	716A>T	Q239L
SORD	U07361	182500	GEN-1DR	Homo sapiens sorbitol dehydrogenase gene, complete cds	1247	1106T>C	3

SORD	U07361	182500	GEN-1DR	1DR	dehydrogenase gene, complete cds	1275	1134T>G	3
SPARC	J03040	182120	GEN-ZC	GEN-ZC	Human SPARC/osteonectin mRNA, complete cds	70	13A>T	I5F
SPARC	J03040	182120	GEN-ZC	GEN-ZC	Human SPARC/osteonectin mRNA, complete cds	123	66A>G	S
SPARC	J03040	182120	GEN-ZC	GEN-ZC	Human SPARC/osteonectin mRNA, complete cds	184	127G>T	V43L
SPARC	J03040	182120	GEN-ZC	GEN-ZC	Human SPARC/osteonectin mRNA, complete cds	559	502C>G	R168G
SPARC	J03040	182120	GEN-ZC	GEN-ZC	Human SPARC/osteonectin mRNA, complete cds	998	941C>G	3
SPARC	J03040	182120	GEN-ZC	GEN-ZC	Human SPARC/osteonectin mRNA, complete cds	1183	1126C>G	3
SPARC	J03040	182120	GEN-ZC	GEN-ZC	Human SPARC/osteonectin mRNA, complete cds	1413	1356G>A	3
SPARC	J03040	182120	GEN-ZC	GEN-ZC	Human SPARC/osteonectin mRNA, complete cds	1551	1494C>G	3
SPARC	J03040	182120	GEN-ZC	GEN-ZC	Human SPARC/osteonectin mRNA, complete cds	1922	1865G>T	3
SPARC	J03040	182120	GEN-ZC	GEN-ZC	Human SPARC/osteonectin mRNA, complete cds	2072	2015T>C	3
SPARC	J03040	182120	GEN-ZC	GEN-ZC	Human SPARC/osteonectin mRNA, complete cds	2092	2035A>G	3
SPARC	J03040	182120	GEN-ZC	GEN-ZC	Human SPARC/osteonectin mRNA, complete cds	2104	2047A>C	3

SPP1	X13694	166490	GEN-1P2	Human mRNA for osteopontin	349	282T>C	S
SPP1	X13694	166490	GEN-1P2	Human mRNA for osteopontin	817	750C>T	S
SPP1	X13694	166490	GEN-1P2	Human mRNA for osteopontin	969	902G>A	R301H
SPP1	X13694	166490	GEN-1P2	Human mRNA for osteopontin	1150	1083A>G	3
SPP1	X13694	166490	GEN-1P2	Human mRNA for osteopontin	1306	1239A>C	3
SRD5A2	M74047	264600	GEN-CDC	Human steroid 5-alpha-reductase 2 (SRD5A2) mRNA, complete cds	2379	2352A>G	3
STAR	U17280	600617	GEN-208	Human steroidogenic acute regulatory protein (STAR) mRNA, complete cds	1439	1313C>T	3
TBG	M14091	314200	GEN-1QO	Human thyroxine-binding globulin mRNA, complete cds	901	571G>A	D191N
TBG	M14091	314200	GEN-1QO	Human thyroxine-binding globulin mRNA, complete cds	1239	909G>T	L303F
TCF14	X76930	600281	GEN-3PH	H.sapiens HNF 4 mRNA for hepatocyte nuclear factor 4	1325	1306C>T	P436S
TF	M12530	190000	GEN-1MK	Human transferrin mRNA, complete cds	654	624G>A	S
TF	M12530	190000	GEN-1MK	Human transferrin mRNA, complete cds	768	738C>G	C246W
TF	M12530	190000	GEN-1MK	Human transferrin mRNA, complete cds	1447	1417G>T	V473F
TF	M12530	190000	GEN-1MK	Human transferrin mRNA, complete cds	1602	1572G>C	S
TF	M12530	190000	GEN-1MK	Human transferrin mRNA, complete cds	1632	1602C>T	S
TF	M12530	190000	GEN-1MK	Human transferrin mRNA, complete cds	1795	1765C>T	P589S
TGFBR2	M85079	190182	GEN-3ZS	Human TGF-beta type II receptor mRNA, complete cds	2045	1710A>C	3
TGFBR3	L07594	600742	GEN-	Human transforming	3966	3618G>C	3

U00968	U00968	184756	GEN-UU	1EA	growth factor-beta type III receptor (TGF-beta) mRNA, complete cds	3983	3817G>A	3
U02031	U02031	600481	GEN-WD		Human SREBP-1 mRNA, complete cds	1089	972G>A	S
U09648	U09648	600650	GEN-1I		Human sterol regulatory element binding protein-2 mRNA, complete cds	2556	2040G>A	3
U09648	U09648	600650	GEN-1I		Carnitine Palmitoyltransferase II	2675	2159G>A	3
U09648	U09648	600650	GEN-1I		Carnitine Palmitoyltransferase II	2792	2276G>A	3
U09648	U09648	600650	GEN-1I		Carnitine Palmitoyltransferase II	2825	2309G>A	3
U09759	U09759	602896	GEN-1HA		Human protein kinase (JNK2) mRNA, complete cds	303	152A>G	N51S
U09759	U09759	602896	GEN-1HA		Human protein kinase (JNK2) mRNA, complete cds	1079	928A>G	I310V
U09759	U09759	602896	GEN-1HA		Human protein kinase (JNK2) mRNA, complete cds	1280	1129C>T	P377S
U09759	U09759	602896	GEN-1HA		Human protein kinase (JNK2) mRNA, complete cds	1559	1408C>T	3
U16031	U16031	None	GEN-HX		Transcription Factor IL-4 Stat	2964	2799G>A	3
U16660	U16660	600696	GEN-1YD		Human peroxisomal enoyl-CoA hydratase-like protein (HPXEL) mRNA, complete cds	149	122A>C	E41A
U16660	U16660	600696	GEN-1YD		Human peroxisomal enoyl-CoA hydratase-like protein (HPXEL) mRNA, complete cds	402	375G>A	S
U16660	U16660	600696	GEN-1YD		Human peroxisomal enoyl-CoA hydratase-like protein (HPXEL) mRNA, complete cds	802	775C>G	P259A

U16660	U16660	600696	GEN-1YD	Human peroxisomal enoyl-CoA hydratase-like protein (HPXEL) mRNA, complete cds	1157	1130G>A	3
U19775	U19775	600289	GEN-22C	Human MAP kinase Mxi2 (MXI2) mRNA, complete cds	731	688G>A	D230N
U24183	U24183	232800	GEN-19	Phosphofructokinase, muscle	70	(-1204)G>A	5
U24183	U24183	232800	GEN-19	Phosphofructokinase, muscle	237	(-1037)G>A	5
U24183	U24183	232800	GEN-19	Phosphofructokinase, muscle	592	(-682)T>C	5
U24183	U24183	232800	GEN-19	Phosphofructokinase, muscle	2662	1389T>G	S
U24183	U24183	232800	GEN-19	Phosphofructokinase, muscle	2953	1680C>T	3
U25029	U25029	138040	GEN-82	Glucocorticoid receptor alpha	335	335C>T	3
U25029	U25029	138040	GEN-82	Glucocorticoid receptor alpha	386	386T>C	3
U25029	U25029	138040	GEN-82	Glucocorticoid receptor alpha	1069	1069C>T	3
U26553	U26553	114131	GEN-66	Calcitonin Receptor	1412	1340C>T	P447L
U26553	U26553	114131	GEN-66	Calcitonin Receptor	1515	1443T>C	3
U32500	U32500	162642	GEN-1P	Neuropeptide Y2	407	159C>T	S
U32500	U32500	162642	GEN-1P	Neuropeptide Y2	833	585T>C	S
U32500	U32500	162642	GEN-1P	Neuropeptide Y2	833	585T>C	S
U32500	U32500	162642	GEN-1P	Neuropeptide Y2	1184	936T>C	S
U32500	U32500	162642	GEN-1P	Neuropeptide Y2	1184	936T>C	S
U32500	U32500	162642	GEN-1P	Neuropeptide Y2	1706	1458-1460TAT>TA	3
U32500	U32500	162642	GEN-1P	Neuropeptide Y2	1706	1458-1460delTAT	3
U32500	U32500	162642	GEN-1P	Neuropeptide Y2	2782	2534^2535ins CA	F
U32989	U32989	191070	GEN-2JH	Human tryptophan oxygenase (TDO) mRNA,	991	927G>A	S

U40002	U40002	151750	GEN-2RH	Human hormone-sensitive lipase testicular isoform mRNA, complete cds	2076	1799C>A	P600H
U40347	U40347	600950	GEN-2RK	Human serotonin N-acetyltransferase mRNA, complete cds	382	148G>A	E50K
U40396	U40396	602691	GEN-6W	Steroid receptor coactivator (SRC-1)	285	229A>C	K77Q
U40396	U40396	602691	GEN-6W	Steroid receptor coactivator (SRC-1)	314	258A>T	K86N
U40396	U40396	602691	GEN-6W	Steroid receptor coactivator (SRC-1)	336	280C>T	P94S
U40396	U40396	602691	GEN-6W	Steroid receptor coactivator (SRC-1)	688	632C>T	T211I
U40396	U40396	602691	GEN-6W	Steroid receptor coactivator (SRC-1)	970	914C>A	A305E
U40396	U40396	602691	GEN-6W	Steroid receptor coactivator (SRC-1)	1511	1455G>A	S
U40396	U40396	602691	GEN-6W	Steroid receptor coactivator (SRC-1)	2377	2321C>T	T774M
U40396	U40396	602691	GEN-6W	Steroid receptor coactivator (SRC-1)	2730	2674C>T	P892S
U41078	U41078	600754	GEN-2SU	Human membrane-type matrix metalloproteinase-1 mRNA, complete cds	22	22C>T	P8S
U43142	U43142	601528	GEN-2UM	Human vascular endothelial growth factor related protein VRP mRNA, complete cds	1499	1128C>T	S
U48730	U48730	601511	GEN-JA	Transcription Factor Stat5b	494	484T>C	S
U48730	U48730	601511	GEN-JA	Transcription Factor Stat5b	496	486A>G	S
U48730	U48730	601511	GEN-JA	Transcription Factor Stat5b	499	489A>G	S
U48730	U48730	601511	GEN-JA	Transcription Factor Stat5b	502	492G>A	S
U48730	U48730	601511	GEN-JA	Transcription Factor Stat5b	570	580G>C	G187A
U48730	U48730	601511	GEN-JA	Transcription Factor Stat5b	573	563C>A	P188Q
U48730	U48730	601511	GEN-JA	Transcription Factor Stat5b	1003	993G>A	S
U48730	U48730	601511	GEN-JA	Transcription Factor Stat5b	1063	1053T>C	S
U48730	U48730	601511	GEN-JA	Transcription Factor Stat5b	1066	1056G>A	S

U48730	U48730	601511	GEN-JA	Transcription Factor Stat5b	1105	1095C>T	S
U48730	U48730	601511	GEN-JA	Transcription Factor Stat5b	1159	1149C>T	S
U48730	U48730	601511	GEN-JA	Transcription Factor Stat5b	1969	1959C>T	S
U49516	U49516	312861	GEN-1Q	Serotonin 5-HT receptors	2915	2187A>C	3
U49516	U49516	312861	GEN-1Q	Serotonin 5-HT receptors	2947	2219A>G	3
U62768	U62768	151300	GEN-3CR	Human oxytocinase splice variant 1 mRNA, complete cds	3356	3295G>C	3
U62768	U62768	151300	GEN-3CR	Human oxytocinase splice variant 1 mRNA, complete cds	3547	3486C>T	3
U71321	U71321	602623	GEN-2TW	Human FK506-binding protein FKBP51 mRNA, complete cds	1248	1095C>T	S
U71321	U71321	602623	GEN-2TW	Human FK506-binding protein FKBP51 mRNA, complete cds	1425	1272G>A	S
U94357	U94357	None	GEN-498	Homo sapiens glycogenin-2 delta (glycogenin-2) mRNA, partial cds	1595	1595C>T	3
U94357	U94357	None	GEN-498	Homo sapiens glycogenin-2 delta (glycogenin-2) mRNA, partial cds	1844	1844A>C	3
UCP2	U76367	601693	GEN-3OV	Human uncoupling protein-2 (UCP2) mRNA, nuclear gene encoding mitochondrial protein, complete cds	164	164C>T	A55V
V00518	V00518	118850	GEN-P4	Human messenger RNA for chorionic gonadotropin	565	515T>C	3
V00519	V00519	139250	GEN-4U	Growth hormone 1	299	259C>A	P87T
V00519	V00519	139250	GEN-4U	Growth hormone 1	524	484G>T	G162W
V00566	V00566	176760	GEN-4V	Prolactin	574	570G>A	S
V00571	V00571	122560	GEN-CBO	corticotropin releasing factor	822	637delA	F
V00571	V00571	122560	GEN-CBO	corticotropin releasing factor	837	652G>A	3
VEGF	M32977	192240	GEN-2JF	Human heparin-binding	50	(-7)C>T	5

VEGF	M32977	192240	GEN-2JF	vascular endothelial growth factor (VEGF) mRNA, complete cds	92	36C>T	S
VLDLR	L20470	192977	GEN-23D	Human heparin-binding vascular endothelial growth factor (VEGF) mRNA, complete cds	336	(-56)C>T	5
VLDLR	L20470	192977	GEN-23D	Human very low density lipoprotein receptor mRNA, complete cds	3566	3175T>C	3
X00264	X00264	152780	GEN-CC2	Human beta-LH gene (luteinizing hormone gene beta subunit)	1015	1016G>C	3
X00264	X00264	152780	GEN-CC2	Human beta-LH gene (luteinizing hormone gene beta subunit)	1033	1034C>A	3
X00568	X00568	207750	GEN-6Z	Apolipoprotein C-II	70	70C>A	Q24K
X02317	X02317	147450	GEN-KM	Superoxide dismutase 1 (Cu/Zn)	614	550A>C	3
X02812	X02812	190180	GEN-XR	Human mRNA for transforming growth factor-beta (TGF-beta)	870	29C>T	P10L
X02812	X02812	190180	GEN-XR	Human mRNA for transforming growth factor-beta (TGF-beta)	979	138C>G	I46M
X02812	X02812	190180	GEN-XR	Human mRNA for transforming growth factor-beta (TGF-beta)	1632	791C>T	T264I
X02812	X02812	190180	GEN-XR	Human mRNA for transforming growth factor-beta (TGF-beta)	1807	966C>T	S
X02812	X02812	190180	GEN-XR	Human mRNA for transforming growth factor-beta (TGF-beta)	1930	1089G>A	S
X02812	X02812	190180	GEN-XR	Human mRNA for transforming growth factor-beta (TGF-beta)	1942	1101C>T	S
X02812	X02812	190180	GEN-XR	Human mRNA for transforming growth factor-beta (TGF-beta)	2013	1172G>A	S391N

X03172	X03172	192340	GEN-ZM	transforming growth factor-beta (TGF-beta)	379	356T>G	V119G
X03635	X03635	133430	GEN-50	Human mRNA for vasopressin precursor	390	30T>C	S
X03635	X03635	133430	GEN-50	estrogen receptors	390	30T>C	S
X03635	X03635	133430	GEN-50	estrogen receptors	424	64G>C	E22Q
X03635	X03635	133430	GEN-50	estrogen receptors	617	257C>T	A86V
X03635	X03635	133430	GEN-50	estrogen receptors	621	261G>C	S
X03635	X03635	133430	GEN-50	estrogen receptors	829	469C>T	F
X03635	X03635	133430	GEN-50	estrogen receptors	1335	975C>G	S
X03635	X03635	133430	GEN-50	estrogen receptors	1335	975C>G	S
X03635	X03635	133430	GEN-50	estrogen receptors	1451	1091T>A	V364E
X03635	X03635	133430	GEN-50	estrogen receptors	1674	1314G>A	M438I
X03635	X03635	133430	GEN-50	estrogen receptors	2142	1782A>G	S
X03635	X03635	133430	GEN-50	estrogen receptors	2354	1994A>G	3
X03635	X03635	133430	GEN-50	estrogen receptors	2550	2190A>C	3
X03635	X03635	133430	GEN-50	estrogen receptors	2733	2373C>G	3
X03635	X03635	133430	GEN-50	estrogen receptors	3181	2821T>C	3
X03635	X03635	133430	GEN-50	estrogen receptors	3338	2978C>T	3
X03635	X03635	133430	GEN-50	estrogen receptors	3652	3292-3294CCT>CC	3
X03635	X03635	133430	GEN-50	estrogen receptors	3652	3292-T	3
X03635	X03635	133430	GEN-50	estrogen receptors	3896	3294delCCT	3
X03635	X03635	133430	GEN-50	estrogen receptors	4378	3536C>A	3
X03635	X03635	133430	GEN-50	estrogen receptors	6287	4018T>C	3
X04409	X04409	139320	GEN-7Q	estrogen receptors	363	5927T>C	3
X04409	X04409	139320	GEN-7Q	Guanine nucleotide binding protein (G protein), alpha stimulating activity	525	351C>T	S
X04409	X04409	139320	GEN-7Q	polypeptide 1	525	513C>T	S
X04409	X04409	139320	GEN-7Q	Guanine nucleotide binding protein (G protein), alpha stimulating activity	967	955C>A	R319S
X04409	X04409	139320	GEN-7Q	polypeptide 1	967	955C>A	R319S
X04409	X04409	139320	GEN-7Q	Guanine nucleotide binding protein (G protein), alpha stimulating activity	967	955C>A	R319S

X04409	X04409	139320	GEN-7Q	Guanine nucleotide binding protein (G protein), alpha stimulating activity	1023	1011C>A	S
X04409	X04409	139320	GEN-7Q	Guanine nucleotide binding protein (G protein), alpha stimulating activity	1083	1071C>T	S
X04409	X04409	139320	GEN-7Q	Guanine nucleotide binding protein (G protein), alpha stimulating activity	1213	1201T>G	3
X04409	X04409	139320	GEN-7Q	Guanine nucleotide binding protein (G protein), alpha stimulating activity	1450	1438A>C	3
X04707	X04707	190160	GEN-CCA	Human c-erb-A mRNA for thyroid hormone receptor	1295	995T>C	I332T
X05199	X05199	173350	GEN-PU	Human mRNA for plasminogen	384	330C>T	S
X05199	X05199	173350	GEN-PU	Human mRNA for plasminogen	825	771C>T	S
X05199	X05199	173350	GEN-PU	Human mRNA for plasminogen	996	942C>T	S
X05199	X05199	173350	GEN-PU	Human mRNA for plasminogen	1137	1083A>G	S
X05199	X05199	173350	GEN-PU	Human mRNA for plasminogen	1485	1431C>T	S
X05199	X05199	173350	GEN-PU	Human mRNA for plasminogen	2340	2286T>G	S
X05199	X05199	173350	GEN-PU	Human mRNA for plasminogen	2532	2478G>A	3
X05199	X05199	173350	GEN-PU	Human mRNA for plasminogen	2606	2552T>G	3
X05344	X05344	116840	GEN-PW	Human mRNA for cathepsin D from oestrogen responsive breast cancer cells	1583	1581C>G	3
X05344	X05344	116840	GEN-PW	Human mRNA for	1703	1701C>T	3

X05344	X05344	116840	GEN-PW	cathepsin D from oestrogen responsive breast cancer cells	1754	1752G>A	3
X05344	X05344	116840	GEN-PW	Human mRNA for cathepsin D from oestrogen responsive breast cancer cells	1798	1796A>C	3
X05344	X05344	116840	GEN-PW	Human mRNA for cathepsin D from oestrogen responsive breast cancer cells	1837	1835A>C	3
X05344	X05344	116840	GEN-PW	Human mRNA for cathepsin D from oestrogen responsive breast cancer cells	1901	1899C>T	3
X05344	X05344	116840	GEN-PW	Human mRNA for cathepsin D from oestrogen responsive breast cancer cells	1975	1973T>G	3
X05615	X05615	188450	GEN-188	Human mRNA for thyroglobulin	5945	5904G>A	S
X05615	X05615	188450	GEN-188	Human mRNA for thyroglobulin	7627	7586G>A	R2529Q
X05615	X05615	188450	GEN-188	Human mRNA for thyroglobulin	7704	7663G>T	V2555F
X05615	X05615	188450	GEN-188	Human mRNA for thyroglobulin	7958	7917C>T	S
X06318	X06318	176970	GEN-KY	Protein kinase C, beta 1	83	(-54)G>C	5
X06318	X06318	176970	GEN-KY	Protein kinase C, beta 1	940	804G>A	S
X06318	X06318	176970	GEN-KY	Protein kinase C, beta 1	1327	1191T>C	S
X06318	X06318	176970	GEN-KY	Protein kinase C, beta 1	1906	1770C>T	S
X06562	X06562	600946	GEN-6D	Growth hormone receptor	3392	3349A>T	3
X06562	X06562	600946	GEN-6D	Growth hormone receptor	4145	4102G>A	3
X07549	X07549	116820	GEN-1DZ	Human mRNA for cathepsin H (E.C.3.4.22.16.)	276	244T>C	3

X07549	X07549	116820	GEN-1DZ	Human mRNA for cathepsin H (E.C.3.4.22.16.)	664	632G>A	3
X07549	X07549	116820	GEN-1DZ	Human mRNA for cathepsin H (E.C.3.4.22.16.)	1006	974G>A	3
X07549	X07549	116820	GEN-1DZ	Human mRNA for cathepsin H (E.C.3.4.22.16.)	1029	997G>A	3
X13589	X13589	107910	GEN-56	Cytochrome P450, subfamily XIX (aromatization of androgens)	364	240A>G	S
X13589	X13589	107910	GEN-56	Cytochrome P450, subfamily XIX (aromatization of androgens)	914	790C>T	R264C
X13589	X13589	107910	GEN-56	Cytochrome P450, subfamily XIX (aromatization of androgens)	914	790C>T	R264C
X13589	X13589	107910	GEN-56	Cytochrome P450, subfamily XIX (aromatization of androgens)	1655	1531C>T	3
X13589	X13589	107910	GEN-56	Cytochrome P450, subfamily XIX (aromatization of androgens)	1796	1672G>T	3
X13629	X13629	107690	GEN-100	Human intestinal mRNA for apolipoprotein A-IV	881	836G>A	R279K
X13629	X13629	107690	GEN-100	Human intestinal mRNA for apolipoprotein A-IV	1185	1140G>T	Q380H
X13629	X13629	107690	GEN-100	Human intestinal mRNA for apolipoprotein A-IV	1302	1257*1258ins CTGT	F
X13916	X13916	107770	GEN-1Q1	Human mRNA for LDL-receptor related protein	1636	1170T>C	S
X13916	X13916	107770	GEN-1Q1	Human mRNA for LDL-receptor related protein	1675	1209C>T	S
X13916	X13916	107770	GEN-1Q1	Human mRNA for LDL-receptor related protein	2805	2339C>T	T780I

X13916	X13916	107770	GEN-1Q1	Human mRNA for LDL-receptor related protein	3853	3387T>C	S
X13916	X13916	107770	GEN-1Q1	Human mRNA for LDL-receptor related protein	6443	5977C>T	R1993W
X13916	X13916	107770	GEN-1Q1	Human mRNA for LDL-receptor related protein	7036	6570C>T	S
X13916	X13916	107770	GEN-1Q1	Human mRNA for LDL-receptor related protein	8608	8142G>A	S
X13916	X13916	107770	GEN-1Q1	Human mRNA for LDL-receptor related protein	8923	8457C>T	S
X13916	X13916	107770	GEN-1Q1	Human mRNA for LDL-receptor related protein	9034	8568G>T	S
X13916	X13916	107770	GEN-1Q1	Human mRNA for LDL-receptor related protein	9040	8574C>T	S
X13916	X13916	107770	GEN-1Q1	Human mRNA for LDL-receptor related protein	9391	8925T>C	S
X15357	X15357	108960	GEN-KUV	Human mRNA for natriuretic peptide receptor (ANP-A receptor)	1066	1023G>C	M341I
X15357	X15357	108960	GEN-KUV	Human mRNA for natriuretic peptide receptor (ANP-A receptor)	1657	1614C>T	S
X15357	X15357	108960	GEN-KUV	Human mRNA for natriuretic peptide receptor (ANP-A receptor)	2859	2816G>A	R939Q
X15357	X15357	108960	GEN-KUV	Human mRNA for natriuretic peptide receptor (ANP-A receptor)	2983	2940G>A	S
X15357	X15357	108960	GEN-KUV	Human mRNA for natriuretic peptide receptor (ANP-A receptor)	3259	3216delC	F
X15357	X15357	108960	GEN-KUV	Human mRNA for natriuretic peptide receptor (ANP-A receptor)	3589	3546*3547ins GAAA	F
X51362	X51362	126450	GEN-31W	Dopamine Receptor D2	588	423G>A	S
X51362	X51362	126450	GEN-31W	Dopamine Receptor D2	1104	939C>T	S
X51362	X51362	126450	GEN-31W	Dopamine Receptor D2	1122	957T>C	S
X51362	X51362	126450	GEN-31W	Dopamine Receptor D2	1248	1083A>G	S

X51362	X51362	126450	31W GEN-31W	Dopamine Receptor D2	1488	1323T>C	S
X51362	X51362	126450	31W GEN-31W	Dopamine Receptor D2	1548	1383A>G	3
X51362	X51362	126450	31W GEN-31W	Dopamine Receptor D2	2361	2196C>T	3
X51416	X51416	601998	GEN-57	STERIOD HORMONE RECEPTOR ERR1	2285	2222G>A	3
X52773	X52773	180245	GEN-74	Retinoid X receptor, alpha	1744	1669G>A	3
X55005	X55005	190120	GEN-35S	Human c-erbA-1 mRNA for thyroid hormone receptor	493	27A>G	S
X55005	X55005	190120	GEN-35S	Human c-erbA-1 mRNA for thyroid hormone receptor alpha	1523	1057G>A	V353I
X59498	X59498	176300	GEN-RU	H.sapiens ttr mRNA for transthyretin	92	71G>A	G24D
X59498	X59498	176300	GEN-RU	H.sapiens ttr mRNA for transthyretin	177	156G>T	S
X59498	X59498	176300	GEN-RU	H.sapiens ttr mRNA for transthyretin	380	359C>T	S120F
X59842	X59842	600214	GEN-3A3	Human PBX2 mRNA	2339	2043T>G	3
X63359	X63359	600070	GEN-3DC	H.sapiens UGT2B10 mRNA for udp glucuronosyltransferase	1516	1506C>T	S
X63359	X63359	600070	GEN-3DC	H.sapiens UGT2B10 mRNA for udp glucuronosyltransferase	2714	2704G>A	3
X63522	X63522	180246	GEN-75	MHC class I promoter binding protein	1331	1152T>C	S
X68596	X68596	168468	GEN-3IJ	H.sapiens mRNA for parathyroid hormone receptor	1563	1389T>C	S
X69141	X69141	184420	GEN-3J9	H.sapiens mRNA for squalene synthase	112	21T>C	S
X69141	X69141	184420	GEN-3J9	H.sapiens mRNA for squalene synthase	292	201C>T	S
X69141	X69141	184420	GEN-3J9	H.sapiens mRNA for squalene synthase	1436	1345T>C	3

X69141	X69141	184420	GEN-3J9	H.sapiens mRNA for squalene synthase	1579	1488T>C	3
X69141	X69141	184420	GEN-3J9	H.sapiens mRNA for squalene synthase	1621	1530C>T	3
X69141	X69141	184420	GEN-3J9	H.sapiens mRNA for squalene synthase	1719	1628A>C	3
X69141	X69141	184420	GEN-3J9	H.sapiens mRNA for squalene synthase	1904	1813G>C	3
X69699	X69699	167415	GEN-3JS	H.sapiens Pax8 mRNA	1412	1413G>C	3
X69699	X69699	167415	GEN-3JS	H.sapiens Pax8 mRNA	2164	2165T>G	3
X69699	X69699	167415	GEN-3JS	H.sapiens Pax8 mRNA	2508	2509T>C	3
X69699	X69699	167415	GEN-3JS	H.sapiens Pax8 mRNA	2514	2515A>C	3
X69699	X69699	167415	GEN-3JS	H.sapiens Pax8 mRNA	2552	2553A>C	3
X70811	X70811	109691	GEN-3KK	beta-3-adrenergic receptor	315	190T>C	W64R
X70811	X70811	109691	GEN-3KK	beta-3-adrenergic receptor	315	190T>C	W64R
X71440	X71440	None	GEN-3KS	H.sapiens mRNA for peroxisomal acyl-CoA oxidase	949	936G>C	M312I
X75958	X75958	600456	GEN-3OE	H.sapiens trkB mRNA for protein-tyrosine kinase	30	(-68)C>G	5
X75958	X75958	600456	GEN-3OE	H.sapiens trkB mRNA for protein-tyrosine kinase	2010	1913A>G	3
X75958	X75958	600456	GEN-3OE	H.sapiens trkB mRNA for protein-tyrosine kinase	2101	2004C>T	3
X76180	X76180	600228	GEN-N5	Solute carrier family 9 (sodium/hydrogen exchanger), isoform 1 (antiporter, Na+/H+, amiloride sensitive)	1901	1802G>A	G601D
X77383	X77383	600550	GEN-3PT	H.sapiens mRNA for cathepsin-O	1595	1546C>T	3
X77533	X77533	602730	GEN-3Q3	H.sapiens mRNA for activin type II receptor	1462	1458C>T	S
X78873	X78873	601792	GEN-	H.sapiens mRNA for	538	535G>A	D179N

X78873	X78873	601792	3RQ GEN-	inhibitor 2 gene	812	809G>A	3
X79483	X79483	602399	3RQ GEN- LPR	H.sapiens mRNA for inhibitor 2 gene H.sapiens ERK6 mRNA for extracellular signal regulated kinase	1287	1254T>G	3
X79537	X79537	603942	GEN- 3TA	H.sapiens mRNA for glycogenin	635	552G>A	S
X79537	X79537	603942	GEN- 3TA	H.sapiens mRNA for glycogenin	1381	1298A>G	3
X83368	X83368	601232	GEN- 3XT	H.sapiens mRNA for phosphatidylinositol 3 kinase gamma	3884	3561C>T	3
X87212	X87212	602365	GEN- 42U	H.sapiens mRNA for cathepsin C	318	285G>T	S
X87212	X87212	602365	GEN- 42U	H.sapiens mRNA for cathepsin C	870	837G>C	Q279H
X87212	X87212	602365	GEN- 42U	H.sapiens mRNA for cathepsin C	1390	1357A>G	I453V
X87212	X87212	602365	GEN- 42U	H.sapiens mRNA for cathepsin C	1758	1725A>C	3
X92521	X92521	601807	GEN-480	H.sapiens mRNA for MMP- 19 protein	1722	1621T>G	3
X92720	X92720	261650	GEN-484	H.sapiens mRNA for phosphoenolpyruvate carboxykinase	1494	1428A>C	R476S
X95190	X95190	601641	GEN- 49Y	H.sapiens mRNA for Branched chain Acyl-CoA Oxidase	1394	1302C>T	S
X95190	X95190	601641	GEN- 49Y	H.sapiens mRNA for Branched chain Acyl-CoA Oxidase	1934	1842C>A	S
Y00285	Y00285	147280	GEN-6I	IGF-2 receptor	4613	4466G>A	S1489N
Y00285	Y00285	147280	GEN-6I	IGF-2 receptor	6371	6224C>T	T2075M
Y00285	Y00285	147280	GEN-6I	IGF-2 receptor	6813	6666C>T	S
Y00285	Y00285	147280	GEN-6I	IGF-2 receptor	7150	7003G>A	V2335M
Y00285	Y00285	147280	GEN-6I	IGF-2 receptor	8685	8538C>A	3
Y00406	Y00406	274500	GEN-6J	Peroxidase (thyroid)	2185	2145T>C	S
Y00406	Y00406	274500	GEN-6J	Peroxidase (thyroid)	2213	2173C>A	P725T
Y00406	Y00406	274500	GEN-6J	Peroxidase (thyroid)	2580	2540C>T	A847V

Y00406	Y00406	274500	GEN-6J	Peroxidase (thyroid)	2923	2883C>G	3
Y00749	Y00749	131240	GEN-P7	Endothelin 1	846	594G>T	K198N
Y08110	Y08110	602005	GEN-1FK	H.sapiens mRNA for mosaic protein LR11	3641	3561T>G	S
Y08110	Y08110	602005	GEN-1FK	H.sapiens mRNA for mosaic protein LR11	3818	3738C>T	S
Y08110	Y08110	602005	GEN-1FK	H.sapiens mRNA for mosaic protein LR11	5158	5078G>A	S1693N
Y08110	Y08110	602005	GEN-1FK	H.sapiens mRNA for mosaic protein LR11	6571	6491G>A	R2164K
Y10055	Y10055	602839	GEN-1IC	H.sapiens mRNA for phosphoinositide 3-kinase	954	758G>A	S253N
Y10055	Y10055	602839	GEN-1IC	H.sapiens mRNA for phosphoinositide 3-kinase	2491	2295C>T	S
Y10055	Y10055	602839	GEN-1IC	H.sapiens mRNA for phosphoinositide 3-kinase	3004	2808C>T	S
Y11525	Y11525	116897	GEN-1KR	H.sapiens mRNA for CCAAT/enhancer binding protein alpha	922	773C>T	A258V
Y11525	Y11525	116897	GEN-1KR	H.sapiens mRNA for CCAAT/enhancer binding protein alpha	1007	858G>A	S
Y11525	Y11525	116897	GEN-1KR	H.sapiens mRNA for CCAAT/enhancer binding protein alpha	1441	1292G>A	3
Y11525	Y11525	116897	GEN-1KR	H.sapiens mRNA for CCAAT/enhancer binding protein alpha	2327	2178T>C	3
Y15409	Y15409	602671	GEN-1U1	Homo sapiens mRNA for putative glucose 6-phosphate translocase	1393	1224G>A	S
Y15409	Y15409	602671	GEN-1U1	Homo sapiens mRNA for putative glucose 6-phosphate translocase	1584	1415C>G	3
Y15409	Y15409	602671	GEN-1U1	Homo sapiens mRNA for putative glucose 6-phosphate translocase	1877	1708C>T	3
Y15521	Y15521	None	GEN-MEN	Homo sapiens ASMTL gene	1622	1622A>G	K541R
Z11695	Z11695	176948	GEN-1L1	H.sapiens 40 kDa protein kinase related to rat ERK2	1287	1153G>A	3

Z11696	Z11696	601795	GEN-1L0	H.sapiens 44kDa protein kinase related to rat ERK1	449	449T>G	1150S
Z82022	Z82022	191350	GEN-3WH	H.sapiens mRNA for GlcNac-1-P transferase	1256	1153A>G	1385V
Z82022	Z82022	191350	GEN-3WH	H.sapiens mRNA for GlcNac-1-P transferase	1491	1388G>A	3
Z82022	Z82022	191350	GEN-3WH	H.sapiens mRNA for GlcNac-1-P transferase	1723	1620T>C	3

Table 17.
Identified
Variances
In Genes
for
Pathways
Identified
in
Endocrine
and
Metabolic
Disease
and
Related
Disorders

AB00026	AB00026	602784	GEN-16N	Human mRNA for prepro cortistatin like peptide, complete cds	215	210T>C	S
AB00102	AB00102	180903	GEN-18S	Homo sapiens mRNA for brain ryanodine receptor, complete cds	14689	14603T>G	3
AB00102	AB00102	180903	GEN-18S	Homo sapiens mRNA for brain ryanodine receptor, complete cds	15521	15435G>A	3
AB00132	AB00132	600170	GEN-KYP	Human AQP3 gene for aquaporine 3 (water channel), partial cds	1203	1143G>A	3
AB00528	AB00528	300135	GEN-KVU	Homo sapiens mRNA for ABC transporter 7 protein, complete cds	2137	2069A>T	H690L
AB00529	AB00529	170290	GEN-W4	Homo sapiens mRNA for	2197	2073A>T	3

AB00942	3	AB00942	600130	GEN-MDN	perilipin, complete cds	1016	534C>T	S
AB01071	6	AB01071	602601	GEN-1SQ	Homo sapiens gene for apobec-1	1071	1010T>A	3
AB01071	0	AB01071	602601	GEN-1SQ	Homo sapiens mRNA for lectin-like oxidized LDL receptor, complete cds	1073	1012T>C	3
AB01071	0	AB01071	602601	GEN-1SQ	Homo sapiens mRNA for lectin-like oxidized LDL receptor, complete cds	1073	1012T>C	3
AB01071	0	AB01071	602601	GEN-1SQ	Homo sapiens mRNA for lectin-like oxidized LDL receptor, complete cds	1801	1740A>G	3
AB01071	0	AB01071	602601	GEN-1SQ	Homo sapiens mRNA for lectin-like oxidized LDL receptor, complete cds	2199	2138G>A	3
AB02068	0	AB02068	None	GEN-LAX	Homo sapiens complete cds	3854	3854A>G	3
AF000234	3	AF000234	600846	GEN-16J	KIAA0873 protein, partial cds	365	365C>T	P122L
AF000234	6	AF000234	600846	GEN-16J	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 4; P2RX4	381	381G>A	S
AF000234	0	AF000234	600846	GEN-16J	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 4; P2RX4	624	624A>G	S
AF000234	0	AF000234	600846	GEN-16J	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 4; P2RX4	641	641C>T	P214L
AF000234	0	AF000234	600846	GEN-16J	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 4; P2RX4	1161	1161T>C	3
AF000571	0	AF000571	192500	GEN-15U	K+ channel (KvLQT1)	545	435C>T	S
AF000571	0	AF000571	192500	GEN-15U	K+ channel (KvLQT1)	1748	1638G>A	S
AF000571	0	AF000571	192500	GEN-15U	K+ channel (KvLQT1)	2360	2250G>A	3

AF000571	AF000571	192500	15U GEN-	K+ channel (KvLQT1)	2552	2442C>T	3
AF000571	AF000571	192500	15U GEN-	K+ channel (KvLQT1)	3016	2906A>G	3
AF000571	AF000571	192500	15U GEN-	K+ channel (KvLQT1)	3073	2963A>G	3
AF001174	AF001174	602898	15U GEN-	Homo sapiens p38beta2 MAP kinase mRNA, complete cds	1044	1038T>C	S
AF004709	AF004709	602899	GEN-UX	Homo sapiens stress- activated protein kinase 4 mRNA, complete cds	432	384G>A	S
AF005043	AF005043	603501	GEN-VX	Homo sapiens poly(ADP- ribose) glycohydrolase (hPARG) mRNA, complete cds	1916	1750G>A	A584T
AF005043	AF005043	603501	GEN-VX	Homo sapiens poly(ADP- ribose) glycohydrolase (hPARG) mRNA, complete cds	3780	3614C>G	3
AF009620	AF009620	601763	GEN- 1HV	Homo sapiens apoptotic caspase Mch5-beta mRNA, alternatively spliced, complete cds	808	808C>G	H270D
AF009620	AF009620	601763	GEN- 1HV	Homo sapiens apoptotic caspase Mch5-beta mRNA, alternatively spliced, complete cds	915	915G>A	S
AF016709	AF016709	602836	GEN- 1NE	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 5; P2RX5	1023	987T>C	S
AF016709	AF016709	602836	GEN- 1NE	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 5; P2RX5	1025	989T>C	F330S
AF016709	AF016709	602836	GEN- 1NE	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 5; P2RX5	1090	1054G>C	E352Q
AF016709	AF016709	602836	GEN- 1NE	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 5; P2RX5	1321	1285G>A	3

AF016709	AF016709	602836	GEN-1NE	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 5; P2RX5	1424	1388C>G	3
AF016709	AF016709	602836	GEN-1NE	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 5; P2RX5	1512	1476G>A	3
AF016709	AF016709	602836	GEN-1NE	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 5; P2RX5	1743	1707A>G	3
AF016709	AF016709	602836	GEN-1NE	PURINERGIC RECEPTOR P2X, LIGAND-GATED ION CHANNEL, 5; P2RX5	1858	1822A>G	3
AF021792	AF021792	603167	GEN-2A5	Homo sapiens Bcl-X/Bcl-2 binding protein (BAD) mRNA, partial cds	781	781G>A	3
AF021792	AF021792	603167	GEN-2A5	Homo sapiens Bcl-X/Bcl-2 binding protein (BAD) mRNA, partial cds	883	883C>A	3
HRH1	AF026261	600167	GEN-26W	Histamine receptor H1 mRNA, partial cds	1068	1068A>G	S
AVPR1B	AF030512	600264	GEN-4FF	Homo sapiens small cell vasopressin subtype 1b receptor mRNA, complete cds	273	150G>A	S
AF030625	AF030625	600821	GEN-2	Vasopressin V1A receptor	314	291C>T	S
AF030625	AF030625	600821	GEN-2	Vasopressin V1A receptor	431	408T>C	S
AF030625	AF030625	600821	GEN-2	Vasopressin V1A receptor	506	483A>G	S
ITGA7	AF032108	600536	GEN-2NO	Homo sapiens integrin alpha-7 mRNA, complete cds	527	366G>A	S
AF033850	AF033850	602384	GEN-2OB	Homo sapiens phospholipase D2 (PLD2) mRNA, complete cds	795	634C>T	R212C
AF033850	AF033850	602384	GEN-2OB	Homo sapiens phospholipase D2 (PLD2) mRNA, complete cds	2531	2370G>A	S
AF033850	AF033850	602384	GEN-2OB	Homo sapiens phospholipase D2 (PLD2) mRNA, complete cds	3290	3129C>T	3
AF037335	AF037335	603263	GEN-2KJ	Homo sapiens carbonic anhydrase precursor (CA	1551	1436G>T	3

AF037335	AF037335	603263	GEN-2KJ	12) mRNA, complete cds Homo sapiens carbonic anhydrase precursor (CA 12) mRNA, complete cds	2442	2327C>T	3
AF038955	AF038955	600874	GEN-LEI	Homo sapiens G protein gamma 5 subunit mRNA, complete cds	490	453A>T	3
AF041381	AF041381	602944	GEN-LG1	Homo sapiens putative transcriptional repressor E2F-6 mRNA, partial cds	1214	1214C>T	3
AF052692	AF052692	603324	GEN-MKO	Homo sapiens connexin 31 (GJB3) mRNA, complete cds	2302	1169A>G	3
AF052692	AF052692	603324	GEN-MKO	Homo sapiens connexin 31 (GJB3) mRNA, complete cds	2438	1305T>C	3
AF052692	AF052692	603324	GEN-MKO	Homo sapiens connexin 31 (GJB3) mRNA, complete cds	2504	1371G>C	3
AF058921	AF058921	None	GEN-LJY	Homo sapiens cytosolic phospholipase A2-gamma mRNA, complete cds	1972	1663G>A	3
AF058921	AF058921	None	GEN-LJY	Homo sapiens cytosolic phospholipase A2-gamma mRNA, complete cds	1989	1680A>T	3
AF064548	AF064548	603506	GEN-KV4	Homo sapiens low-density lipoprotein receptor-related protein 5 (LRP5) mRNA, complete cds	1695	1647C>T	S
AF064548	AF064548	603506	GEN-KV4	Homo sapiens low-density lipoprotein receptor-related protein 5 (LRP5) mRNA, complete cds	4037	3989C>T	A1330V
AF064548	AF064548	603506	GEN-KV4	Homo sapiens low-density lipoprotein receptor-related protein 5 (LRP5) mRNA, complete cds	4683	4635C>A	S
AF064548	AF064548	603506	GEN-KV4	Homo sapiens low-density lipoprotein receptor-related protein 5 (LRP5) mRNA, complete cds	4802	4754C>T	S1585L

AF084040	AF084040	107940	GEN- LQ9	Homo sapiens beta-arrestin 1A mRNA, complete cds	986	986A>T	E329V
AF084040	AF084040	107940	GEN- LQ9	Homo sapiens beta-arrestin 1A mRNA, complete cds	1279	1279G>A	3
AJ005162	AJ005162	600067	GEN- KVT	Homo sapiens mRNA for UDP-glucuronosyltransferase	1915	1882A>C	3
AJ224538	AJ224538	602741	GEN-243	Homo sapiens mRNA for AMP-activated protein kinase beta 2 subunit	631	631C>T	H211Y
D00017	D00017	151740	GEN-2D	Lipocortin II (Annexin II)	149	100G>A	D34N
D00017	D00017	151740	GEN-2D	Lipocortin II (Annexin II)	341	292G>T	V98L
D00017	D00017	151740	GEN-2D	Lipocortin II (Annexin II)	479	430A>T	N144Y
D00017	D00017	151740	GEN-2D	Lipocortin II (Annexin II)	1288	1239G>A	3
ATP1A1	D00099	182310	GEN-4E8	Homo sapiens mRNA for Na,K-ATPase alpha-subunit, complete cds	1059	741A>C	S
ATP1A1	D00099	182310	GEN-4E8	Homo sapiens mRNA for Na,K-ATPase alpha-subunit, complete cds	1059	741A>C	S
ATP1A1	D00099	182310	GEN-4E8	Homo sapiens mRNA for Na,K-ATPase alpha-subunit, complete cds	1428	1110G>A	S
ATP1A1	D00099	182310	GEN-4E8	Homo sapiens mRNA for Na,K-ATPase alpha-subunit, complete cds	2538	2220T>C	S
ATP1A1	D00099	182310	GEN-4E8	Homo sapiens mRNA for Na,K-ATPase alpha-subunit, complete cds	3324	3006C>T	S
ATP1A1	D00099	182310	GEN-4E8	Homo sapiens mRNA for Na,K-ATPase alpha-subunit, complete cds	3375	3057G>A	S
ATP1A1	D00099	182310	GEN-4E8	Homo sapiens mRNA for Na,K-ATPase alpha-subunit, complete cds	3397	3079G>A	3
ATP1A1	D00099	182310	GEN-4E8	Homo sapiens mRNA for Na,K-ATPase alpha-subunit, complete cds	3408	3090C>A	3

ATP1A1	D00099	182310	GEN-4E8	Homo sapiens mRNA for Na,K-ATPase alpha-subunit, complete cds	3505	3187C>A	3
ATP1A1	D00099	182310	GEN-4E8	Homo sapiens mRNA for Na,K-ATPase alpha-subunit, complete cds	3538	3220G>T	3
FECH	D00726	177000	GEN-UB	Human mRNA for ferrochelatase (EC 4.99.1.1)	827	798G>C	S
FECH	D00726	177000	GEN-UB	Human mRNA for ferrochelatase (EC 4.99.1.1)	1253	1224T>A	N408K
FECH	D00726	177000	GEN-UB	Human mRNA for ferrochelatase (EC 4.99.1.1)	1549	1520C>T	3
FECH	D00726	177000	GEN-UB	Human mRNA for ferrochelatase (EC 4.99.1.1)	1645	1616G>A	3
D13138	D13138	179780	GEN-1NW	Human mRNA for dipeptidase	566	523T>G	S175A
CYP11B2	D13752	124080	GEN-CCD	Human CYP11B2 gene for steroid 18-hydroxylase, complete cds	1600	1593G>A	3
D14874	D14874	103275	GEN-1SG	Human mRNA for adrenomedullin, complete cds	1293	1137A>G	3
D14874	D14874	103275	GEN-1SG	Human mRNA for adrenomedullin, complete cds	1394	1238A>C	3
HADHB	D16481	143450	GEN-1Y5	Human mRNA for mitochondrial 3-ketoacyl-CoA thiolase beta-subunit of trifunctional protein, complete cds	871	825T>C	S
HADHB	D16481	143450	GEN-1Y5	Human mRNA for mitochondrial 3-ketoacyl-CoA thiolase beta-subunit of trifunctional protein, complete cds	1607	1561G>C	3
HADHB	D16481	143450	GEN-1Y5	Human mRNA for mitochondrial 3-ketoacyl-CoA thiolase beta-subunit of trifunctional protein, complete cds	1908	1862A>C	3

HADHB	D16481	143450	GEN-1Y5	CoA thiolase beta-subunit of trifunctional protein, complete cds Human mRNA for mitochondrial 3-ketoacyl-CoA thiolase beta-subunit of trifunctional protein, complete cds	1911	1865A>C	3
D21243	D21243	141251	GEN-9C	Heme oxygenase (decycling) 2	828	828C>G	S
D25235	D25235	104221	GEN-3	Adrenergic receptor alpha 1c	1035	599T>G	I200S
D25235	D25235	104221	GEN-3	Adrenergic receptor alpha 1c	1475	1039C>T	R347C
D25235	D25235	104221	GEN-3	Adrenergic receptor alpha 1c	1475	1039C>T	R347C
D25235	D25235	104221	GEN-3	Adrenergic receptor alpha 1c	2048	1612C>T	3
D25418	D25418	600022	GEN-78	Prostaglandin I2 (prostaglandin) receptor (IP)	726	635G>A	R212H
D25418	D25418	600022	GEN-78	Prostaglandin I2 (prostaglandin) receptor (IP)	1047	956C>G	S319W
D25418	D25418	600022	GEN-78	Prostaglandin I2 (prostaglandin) receptor (IP)	1075	984A>C	S
PTGIR	D38128	600022	GEN-4DH	Human IP gene for prostacyclin receptor, exon 3	203	204C>G	3
PTGIR	D38128	600022	GEN-4DH	Human IP gene for prostacyclin receptor, exon 3	231	232C>A	3
D38145	D38145	601699	GEN-4E3	Human mRNA for prostacyclin synthase, complete cds	1646	1619T>C	3
D42108	D42108	600597	GEN-2U4	Phospholipase C epsilon	1908	1705G>A	V559I
D42108	D42108	600597	GEN-2U4	Phospholipase C epsilon	2864	2661G>A	S
D42108	D42108	600597	GEN-2U4	Phospholipase C epsilon	4453	4250G>A	3
D45906	D45906	601988	GEN-2WP	Human mRNA for LIMK-2, complete cds	1323	1209G>C	S

D45906	D45906	601988	GEN-2WP	Human mRNA for LIMK-2, complete cds	1475	1361C>T	S454L
D49394	D49394	182139	GEN-5	Serotonin 5-HT receptors 5-HT3	1914	1695C>G	3
D50678	D50678	602600	GEN-30Y	Human mRNA for apolipoprotein E receptor 2, complete cds	3378	3276G>A	3
D50678	D50678	602600	GEN-30Y	Human mRNA for apolipoprotein E receptor 2, complete cds	3755	3653G>A	3
D50678	D50678	602600	GEN-30Y	Human mRNA for apolipoprotein E receptor 2, complete cds	3949	3847G>C	3
D50678	D50678	602600	GEN-30Y	Human mRNA for apolipoprotein E receptor 2, complete cds	4368	4266T>A	3
D50678	D50678	602600	GEN-30Y	Human mRNA for apolipoprotein E receptor 2, complete cds	4455	4353G>A	3
D67031	D67031	601568	GEN-3HA	Homo sapiens ADDL mRNA for adducin-like protein, complete cds	1441	1258G>A	V420M
D67031	D67031	601568	GEN-3HA	Homo sapiens ADDL mRNA for adducin-like protein, complete cds	2782	2599T>C	3
D87258	D87258	602194	GEN-42R	Homo sapiens mRNA for serin protease with IGF-binding motif, complete cds	150	102C>T	S
D87461	D87461	601931	GEN-43N	Human mRNA for KIAA0271 gene, complete cds	2432	2256C>A	3
D87812	D87812	600528	GEN-6	Carnitine Palmitoyltransferase I (muscle)	2363	2344T>C	3
D87845	D87845	602344	GEN-44C	Human mRNA for platelet-activating factor acetylhydrolase 2, complete cds	2299	2096G>A	3
D87845	D87845	602344	GEN-44C	Human mRNA for platelet-activating factor acetylhydrolase 2, complete cds	2332	2129A>G	3

D89078	D89078	601531	GEN-7	complete cds	P2Y7 purinoceptor	434	(-1284)A>T	5
D89078	D89078	601531	GEN-7		P2Y7 purinoceptor	889	(-829)G>C	5
D89078	D89078	601531	GEN-7		P2Y7 purinoceptor	1156	(-562)G>C	5
D89078	D89078	601531	GEN-7		P2Y7 purinoceptor	2644	927T>C	S
D89078	D89078	601531	GEN-7		P2Y7 purinoceptor	2920	1203A>G	3
LRP1	D90070	107770	GEN-466		Human ATL-derived PMA-responsive (APR) peptide mRNA	686	513T>G	3
D90187	D90187	153622	GEN-6M		Macrophage scavenger receptor 1	1414	1388T>G	3
D90187	D90187	153622	GEN-6M		Macrophage scavenger receptor 1	1532	1486A>G	3
D90187	D90187	153622	GEN-6M		Macrophage scavenger receptor 1	1558	1512G>A	3
D90187	D90187	153622	GEN-6M		Macrophage scavenger receptor 1	1599	1553A>G	3
D90187	D90187	153622	GEN-6M		Macrophage scavenger receptor 1	1642	1596T>C	3
D90187	D90187	153622	GEN-6M		Macrophage scavenger receptor 1	1689	1643G>C	3
D90228	D90228	203750	GEN-46A		ACAT1	547	471C>A	S
EDNRA	D90348	131243	GEN-4DX		Endothelin Receptor Type A	1449	969C>T	S
EDNRA	D90348	131243	GEN-4DX		Endothelin Receptor Type A	1449	969C>T	S
EDNRA	D90348	131243	GEN-4DX		Endothelin Receptor Type A	1485	1005A>G	S
EDNRA	D90348	131243	GEN-4DX		Endothelin Receptor Type A	1485	1005A>G	S
EDNRA	D90348	131243	GEN-4DX		Endothelin Receptor Type A	1834	1354C>G	3
EDNRA	D90348	131243	GEN-4DX		Endothelin Receptor Type A	1834	1354C>G	3
EDNRA	D90348	131243	GEN-4DX		Endothelin Receptor Type A	2228	1748G>A	3
EDNRA	D90348	131243	GEN-4DX		Endothelin Receptor Type A	2376	1896G>A	3
EDNRA	D90348	131243	GEN-4DX		Endothelin Receptor Type A	2764	2284G>A	3

EDNRA	D90348	131243	4DX GEN-4DX	Endothelin Receptor Type A	2764	2284G>A	3
EDNRA	D90348	131243	4DX GEN-4DX	Endothelin Receptor Type A	2840	2360G>C	3
EDNRA	D90348	131243	4DX GEN-4DX	Endothelin Receptor Type A	2935	2455G>A	3
EDNRA	D90348	131243	4DX GEN-4DX	Endothelin Receptor Type A	3294	2814A>G	3
FGA	J00127	134820	GEN-T3	Human fibrinogen alpha-chain mRNA, complete cds	560	530T>A	1177N
FGA	J00127	134820	GEN-T3	Human fibrinogen alpha-chain mRNA, complete cds	1138	1108G>T	A370S
J00129	J00129	134830	GEN-T4	Human fibrinogen beta-chain mRNA, partial cds	543	543C>T	S
J00129	J00129	134830	GEN-T4	Human fibrinogen beta-chain mRNA, partial cds	1101	1101C>T	S
J00129	J00129	134830	GEN-T4	Human fibrinogen beta-chain mRNA, partial cds	1409	1409G>A	R470K
J00137	J00137	306900	GEN-OX	COAGULATION FACTOR IX	581	580A>G	T194A
J00277	J00277	190020	GEN-MH8	Human (genomic clones lambda-[SK2-T2, HS578T]; cDNA clones RS-[3, 4, 6]) c-Ha-ras1 proto-oncogene, complete coding sequence	81	81T>C	S
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	1931	1853T>C	V618A
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	6616	6538C>T	F
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	7014	6936T>C	S
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	7623	7545T>C	S
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	8294	8216C>T	P2739L
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	8625	8547T>C	S
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	10033	9955G>C	D3319H
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	10358	10280C>A	T3427K

J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	10372	10294C>G	Q3432E
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	11273	11195T>C	I3732T
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	11705	11627C>T	A3876V
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	11862	11784T>A	S
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	11923	11845T>C	F3949L
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	12461	12383A>T	E4128V
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	12476	12398G>C	G4133A
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	12486	12408G>C	S
J02610	J02610	107730	GEN-6N	Apolipoprotein B (including Ag(x) antigen)	12619	12541G>A	E4181K
J02611	J02611	107740	GEN-6O	Human apolipoprotein D mRNA, complete cds	676	615T>G	3
J02611	J02611	107740	GEN-6O	Human apolipoprotein D mRNA, complete cds	683	622T>G	3
J02611	J02611	107740	GEN-6O	Human apolipoprotein D mRNA, complete cds	701	640C>G	3
J02611	J02611	107740	GEN-6O	Human apolipoprotein D mRNA, complete cds	745	684A>G	3
J03004	J03004	139360	GEN-79	Guanine nucleotide binding protein (G protein), alpha inhibiting activity polypeptide 2	758	681C>T	S
GNAI1	J03005	139370	GEN-ZI	Human alternative guanine nucleotide-binding regulatory protein (G) alpha-inhibitory-subunit mRNA, complete cds	1437	1429G>A	3
J03019	J03019	109630	GEN-4D6	Human beta-1-adrenergic receptor mRNA, complete cds	503	417G>A	S
J03037	J03037	259730	GEN-2I	Carbonic anhydrase II	627	562C>T	S
J03037	J03037	259730	GEN-2I	Carbonic anhydrase II	1334	1269A>C	3

J03037	J03037	259730	GEN-2I	Carbonic anhydrase II	1487	1422A>C	3
J03048	J03048	142290	GEN-ZD	Huma hemopexin mRNA, 3 end	244	244C>T	R82W
J03048	J03048	142290	GEN-ZD	Huma hemopexin mRNA, 3 end	635	635G>A	R212K
J03225	J03225	152310	GEN-ZZ	Human lipoprotein-associated coagulation inhibitor mRNA, complete cds	1189	1057G>A	3
J03242	J03242	147470	GEN-PJ	Insulin-like growth factor 2	932	380G>A	R127H
J03242	J03242	147470	GEN-PJ	Insulin-like growth factor 2	1063	511G>A	A171T
J03242	J03242	147470	GEN-PJ	Insulin-like growth factor 2	1190	638C>G	3
J03242	J03242	147470	GEN-PJ	Insulin-like growth factor 2	1201	649C>T	3
J03250	J03250	172420	GEN-C4	DNA topoisomerase I	160	(-52)C>T	5
J03250	J03250	172420	GEN-C4	DNA topoisomerase I	590	379G>A	V127I
J03250	J03250	172420	GEN-C4	DNA topoisomerase I	1984	1773G>A	S
J03260	J03260	139160	GEN-7A	Guanine nucleotide binding protein (G protein), alpha 2 polypeptide	1491	1479A>G	3
J03260	J03260	139160	GEN-7A	Guanine nucleotide binding protein (G protein), alpha 2 polypeptide	2541	2529T>C	3
J03459	J03459	151570	GEN-8	Leukotriene A4 hydrolase	140	72G>T	S
J03459	J03459	151570	GEN-8	Leukotriene A4 hydrolase	1511	1443A>T	E481D
C7	J03507	217070	GEN-11R	Human complement protein component C7 mRNA, complete cds	1951	1951G>A	V651I
C7	J03507	217070	GEN-11R	Human complement protein component C7 mRNA, complete cds	3032	3032T>C	3
C7	J03507	217070	GEN-11R	Human complement protein component C7 mRNA, complete cds	3634	3634A>G	3
C7	J03507	217070	GEN-11R	Human complement protein component C7 mRNA, complete cds	3831	3831A>G	3
LIPC	J03540	151670	GEN-11J	Human hepatic lipase mRNA, complete cds	469	465T>G	S
LIPC	J03540	151670	GEN-11J	Human hepatic lipase mRNA, complete cds	595	591A>G	S

LIPC	J03540	151670	GEN-11J	Human hepatic lipase mRNA, complete cds	648	644G>A	S215N
LIPC	J03540	151670	GEN-11J	Human hepatic lipase mRNA, complete cds	817	813C>T	S
LIPC	J03540	151670	GEN-11J	Human hepatic lipase mRNA, complete cds	1441	1437C>A	S
J03571	J03571	152390	GEN-9	Lipoxygenases: 5- lipoxygenase (leukocytes)	55	21C>T	S
J03571	J03571	152390	GEN-9	Lipoxygenases: 5- lipoxygenase (leukocytes)	304	270G>A	S
J03571	J03571	152390	GEN-9	Lipoxygenases: 5- lipoxygenase (leukocytes)	304	270G>A	S
J03571	J03571	152390	GEN-9	Lipoxygenases: 5- lipoxygenase (leukocytes)	959	925C>A	P309T
J03571	J03571	152390	GEN-9	Lipoxygenases: 5- lipoxygenase (leukocytes)	1762	1728A>T	S
J03571	J03571	152390	GEN-9	Lipoxygenases: 5- lipoxygenase (leukocytes)	2076	2042- 2043AC>AC	3
J03571	J03571	152390	GEN-9	Lipoxygenases: 5- lipoxygenase (leukocytes)	2076	2042- 2043delAC	F
J03571	J03571	152390	GEN-9	Lipoxygenases: 5- lipoxygenase (leukocytes)	2328	2294C>T	3
J03571	J03571	152390	GEN-9	Lipoxygenases: 5- lipoxygenase (leukocytes)	2376	2342T>G	3
J03853	J03853	104250	GEN-A	Adrenergic receptor alpha 2c	1202	1164C>T	S
J03853	J03853	104250	GEN-A	Adrenergic receptor alpha 2c	1237	1199T>G	I400S
J03853	J03853	104250	GEN-A	Adrenergic receptor alpha 2c	1372	1334C>G	P445R
J03853	J03853	104250	GEN-A	Adrenergic receptor alpha 2c	1379	1341C>T	S
C1S	J04080	120580	GEN- 13T	Complement C1S component precursor (C1 esterase)	558	356G>A	R119H
C1S	J04080	120580	GEN- 13T	Complement C1S component precursor (C1 esterase)	2140	1938A>T	K646N
C1S	J04080	120580	GEN- 13T	Complement C1S component precursor (C1 esterase)	2234	2032A>T	T678S

C1S	J04080	120580	GEN-13T	Complement C1S component precursor (C1 esterase)	2333	2131G>T	3
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	501	479A>G	N160S
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	604	582C>T	S
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	803	781G>T	A261S
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	1042	1020C>T	S
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	1535	1513-1515CCT>CC	S
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	1535	1513-1515delCCT	[P505V;50 6-505del]
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	1797	1775A>G	D592G
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	2215	2193G>A	S
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	2350	2328A>G	S
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	2505	2483T>C	M828T
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	3409	3387T>C	S
J04144	J04144	106180	GEN-2L	Angiotensin-converting enzyme (ACE)	3409	3387T>C	S
C6	J05064	217050	GEN-16S	Human complement component C6 mRNA, complete cds	3281	3126G>A	3
J05096	J05096	182340	GEN-SL	alpha-subunit of Na+/K+ ATPase isoform2	2364	2260T>G	S754A
J05096	J05096	182340	GEN-SL	alpha-subunit of Na+/K+ ATPase isoform2	5295	5191G>A	3
J05158	J05158	603104	GEN-173	Human carboxypeptidase N mRNA, 3 end	2314	2314C>T	3
J05158	J05158	603104	GEN-173	Human carboxypeptidase N mRNA, 3 end	2316	2316G>T	3
J05158	J05158	603104	GEN-173	Human carboxypeptidase N mRNA, 3 end	2332	2332G>T	3

J05158	J05158	603104	GEN-173	N mRNA, 3 end Human carboxypeptidase	2541	2541G>A	3
J05158	J05158	603104	GEN-173	N mRNA, 3 end Human carboxypeptidase	2651	2651C>T	3
J05480	J05480	114105	GEN-D	N mRNA, 3 end Calcineurin A	834	834A>G	3
M6PR	J05550	153618	GEN-180	Human mannose receptor	4890	4787T>A	3
J05594	J05594	601688	GEN-E	mRNA, complete cds Prostaglandin 15-OH	173	156A>G	S
J05594	J05594	601688	GEN-E	dehydrogenase (PGDH) Prostaglandin 15-OH	913	896C>G	3
J05594	J05594	601688	GEN-E	dehydrogenase (PGDH) Prostaglandin 15-OH	950	933G>A	3
J05594	J05594	601688	GEN-E	dehydrogenase (PGDH) Prostaglandin 15-OH	1448	1431G>A	3
J05594	J05594	601688	GEN-E	dehydrogenase (PGDH) Prostaglandin 15-OH	1972	1955T>C	3
J05594	J05594	601688	GEN-E	dehydrogenase (PGDH) Prostaglandin 15-OH	1972	1955T>C	3
K00396	K00396	107741	GEN-P0	dehydrogenase (PGDH) Human apolipoprotein E (epsilon 2 and 3 alleles)	112	52G>A	A18T
K00396	K00396	107741	GEN-P0	mRNA Human apolipoprotein E (epsilon 2 and 3 alleles)	121	61G>A	E21K
K00396	K00396	107741	GEN-P0	mRNA Human apolipoprotein E (epsilon 2 and 3 alleles)	151	91G>A	E31K
K00396	K00396	107741	GEN-P0	mRNA Human apolipoprotein E (epsilon 2 and 3 alleles)	197	137T>C	L46P
K00396	K00396	107741	GEN-P0	mRNA Human apolipoprotein E (epsilon 2 and 3 alleles)	204	144delG	F
K00396	K00396	107741	GEN-P0	mRNA Human apolipoprotein E (epsilon 2 and 3 alleles)	238	178A>G	T60A
K00396	K00396	107741	GEN-P0	mRNA Human apolipoprotein E (epsilon 2 and 3 alleles)	365	305C>G	P102R

K00396	K00396	107741	GEN-P0	Human apolipoprotein E 409 (epsilon 2 and 3 alleles) mRNA	349G>A	A117T
K00396	K00396	107741	GEN-P0	Human apolipoprotein E 448 (epsilon 2 and 3 alleles) mRNA	388T>C	C130R
K00396	K00396	107741	GEN-P0	Human apolipoprotein E 494 (epsilon 2 and 3 alleles) mRNA	434G>A	G145D
K00396	K00396	107741	GEN-P0	Human apolipoprotein E 515 (epsilon 2 and 3 alleles) mRNA	455G>A	R152Q
K00396	K00396	107741	GEN-P0	Human apolipoprotein E 520 (epsilon 2 and 3 alleles) mRNA	460C>A	R154S
K00396	K00396	107741	GEN-P0	Human apolipoprotein E 538 (epsilon 2 and 3 alleles) mRNA	478C>T	R160C
K00396	K00396	107741	GEN-P0	Human apolipoprotein E 547 (epsilon 2 and 3 alleles) mRNA	487C>T	R163C
K00396	K00396	107741	GEN-P0	Human apolipoprotein E 548 (epsilon 2 and 3 alleles) mRNA	488G>A	R163H
K00396	K00396	107741	GEN-P0	Human apolipoprotein E 550 (epsilon 2 and 3 alleles) mRNA	490A>G	K164E
K00396	K00396	107741	GEN-P0	Human apolipoprotein E 586 (epsilon 2 and 3 alleles) mRNA	526C>T	R176C
K00396	K00396	107741	GEN-P0	Human apolipoprotein E 586 (epsilon 2 and 3 alleles) mRNA	526C>T	R176C
K00396	K00396	107741	GEN-P0	Human apolipoprotein E 743 (epsilon 2 and 3 alleles) mRNA	683G>A	F
K00396	K00396	107741	GEN-P0	Human apolipoprotein E 785 (epsilon 2 and 3 alleles) mRNA	725G>A	R242Q
K00396	K00396	107741	GEN-P0	Human apolipoprotein E 796 (epsilon 2 and 3 alleles) mRNA	736C>T	R246C

K00396	K00396	107741	GEN-P0	Human apolipoprotein E 821 (epsilon 2 and 3 alleles) mRNA	761T>A	V254E
K00396	K00396	107741	GEN-P0	Human apolipoprotein E 865 (epsilon 2 and 3 alleles) mRNA	805C>G	R269G
K00396	K00396	107741	GEN-P0	Human apolipoprotein E 935 (epsilon 2 and 3 alleles) mRNA	875G>A	R292H
K00396	K00396	107741	GEN-P0	Human apolipoprotein E 1000 (epsilon 2 and 3 alleles) mRNA	940A>C	S314R
K01911	K01911	162640	GEN-2O	Neuropeptide Y 236 mRNA	150G>A	S
K01911	K01911	162640	GEN-2O	Neuropeptide Y 290 mRNA	204C>T	S
AGT	K02215	106150	GEN-WK	Human angiotensinogen 659 mRNA, complete CDS	620C>T	T207M
AGT	K02215	106150	GEN-WK	Human angiotensinogen 842 mRNA, complete CDS	803T>C	M268T
AGT	K02215	106150	GEN-WK	Human angiotensinogen 1155 mRNA, complete CDS	1116G>A	S
AGT	K02215	106150	GEN-WK	Human angiotensinogen 1476 mRNA, complete CDS	1437C>A	S
AGT	K02215	106150	GEN-WK	Human angiotensinogen 1821 mRNA, complete CDS	1782G>A	3
AGT	K02215	106150	GEN-WK	Human angiotensinogen 2053 mRNA, complete CDS	2014A>C	3
K02286	K02286	191840	GEN-SQ	Human urokinase gene, 3 260 end	260C>G	A87G
K02286	K02286	191840	GEN-SQ	Human urokinase gene, 3 449 end	449G>C	+150S
K02286	K02286	191840	GEN-SQ	Human urokinase gene, 3 887 end	887A>G	Y296C
K02286	K02286	191840	GEN-SQ	Human urokinase gene, 3 902 end	902C>A	P301H
K02286	K02286	191840	GEN-SQ	Human urokinase gene, 3 905 end	905A>G	N302S
KNG	K02566	228960	GEN-X2	Human alpha-2-thiol 1248 proteinase inhibitor mRNA, complete coding sequence	1199C>A	T400K
K02765	K02765	120700	GEN-XM	Human complement 1001	941T>C	L314P

K02765	K02765	120700	GEN-XM	component C3 mRNA, alpha and beta subunits, complete cds	2575	2515G>A	V839I
K02765	K02765	120700	GEN-XM	Human complement component C3 mRNA, alpha and beta subunits, complete cds	3108	3048C>T	S
K02765	K02765	120700	GEN-XM	Human complement component C3 mRNA, alpha and beta subunits, complete cds	3561	3501C>G	S
K02765	K02765	120700	GEN-XM	Human complement component C3 mRNA, alpha and beta subunits, complete cds	4371	4311C>T	S
K02765	K02765	120700	GEN-XM	Human complement component C3 mRNA, alpha and beta subunits, complete cds	4544	4484C>A	P1495Q
K02765	K02765	120700	GEN-XM	Human complement component C3 mRNA, alpha and beta subunits, complete cds	4938	4878T>C	S
K02765	K02765	120700	GEN-XM	Human complement component C3 mRNA, alpha and beta subunits, complete cds	4956	4896T>C	S
K02770	K02770	147720	GEN-5M	complete cds	19	(-68)A>C	5
K02770	K02770	147720	GEN-5M	Interleukin 1, beta	26	(-61)A>C	5
K02770	K02770	147720	GEN-5M	Interleukin 1, beta	48	(-39)C>T	5
K02770	K02770	147720	GEN-5M	Interleukin 1, beta	114	28G>A	E10K
K02770	K02770	147720	GEN-5M	Interleukin 1, beta	119	33G>A	M11I
L00352	L00352	143890	GEN- 2S8	Human low density lipoprotein receptor gene, exon 18	71	72C>T	3
L00352	L00352	143890	GEN-	Human low density	103	104G>A	3

L00352	L00352	143890	2S8	lipoprotein receptor gene, exon 18	717C>T	3
L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	882G>A	3
L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	1181A>G	3
L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	1187C>G	3
L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	1188T>G	3
L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	1192G>A	3
L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	1223G>A	3
L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	1224C>T	3
L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	1225G>A	3
L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	1228T>C	3
L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	1235T>C	3
L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	1253A>T	3
L00352	L00352	143890	GEN-2S8	Human low density lipoprotein receptor gene, exon 18	1269A>C	3

L00352	L00352	143890	GEN- 2S8	Human low density lipoprotein receptor gene, exon 18	1268	1269A>T	3
L00352	L00352	143890	GEN- 2S8	Human low density lipoprotein receptor gene, exon 18	1279	1280C>T	3
L00352	L00352	143890	GEN- 2S8	Human low density lipoprotein receptor gene, exon 18	1280	1281G>A	3
L00352	L00352	143890	GEN- 2S8	Human low density lipoprotein receptor gene, exon 18	1308	1309C>T	3
L00352	L00352	143890	GEN- 2S8	Human low density lipoprotein receptor gene, exon 18	1309	1310G>A	3
L00352	L00352	143890	GEN- 2S8	Human low density lipoprotein receptor gene, exon 18	1316	1317G>A	3
L00352	L00352	143890	GEN- 2S8	Human low density lipoprotein receptor gene, exon 18	1320	1321T>C	3
L00352	L00352	143890	GEN- 2S8	Human low density lipoprotein receptor gene, exon 18	1345	1346G>A	3
L00352	L00352	143890	GEN- 2S8	Human low density lipoprotein receptor gene, exon 18	1368	1369T>C	3
L00352	L00352	143890	GEN- 2S8	Human low density lipoprotein receptor gene, exon 18	1376	1377C>T	3
L00352	L00352	143890	GEN- 2S8	Human low density lipoprotein receptor gene, exon 18	1383	1384C>T	3
L00352	L00352	143890	GEN- 2S8	Human low density lipoprotein receptor gene, exon 18	1406	1407T>C	3
L00352	L00352	143890	GEN- 2S8	Human low density lipoprotein receptor gene, exon 18	1418	1419G>C	3
L00352	L00352	143890	GEN- 2S8	Human low density lipoprotein receptor gene, exon 18	1428	1429T>C	3

L00352	L00352	143890	GEN-2S8	exon 18 Human low density lipoprotein receptor gene,	1453	1454C>T	3
L00352	L00352	143890	GEN-2S8	exon 18 Human low density lipoprotein receptor gene,	1796	1797T>C	3
L00352	L00352	143890	GEN-2S8	exon 18 Human low density lipoprotein receptor gene,	2108	2109G>A	3
L00352	L00352	143890	GEN-2S8	exon 18 Human low density lipoprotein receptor gene,	2490	2491A>C	3
CBS	L00972	236200	GEN-UV	exon 18 Human cystathionine-beta-synthase (CBS) mRNA	1022	1023T>C	3
CBS	L00972	236200	GEN-UV	Human cystathionine-beta-synthase (CBS) mRNA	2001	2002C>T	3
CBS	L00972	236200	GEN-UV	Human cystathionine-beta-synthase (CBS) mRNA	2278	2279G>A	3
CBS	L00972	236200	GEN-UV	Human cystathionine-beta-synthase (CBS) mRNA	2358	2359G>C	3
CBS	L00972	236200	GEN-UV	Human cystathionine-beta-synthase (CBS) mRNA	2524	2525T>C	3
CBS	L00972	236200	GEN-UV	Human cystathionine-beta-synthase (CBS) mRNA	2545	2546C>T	3
L01087	L01087	600448	GEN-CM	Protein kinase C-theta	1940	1846C>A	S
L01087	L01087	600448	GEN-CM	Protein kinase C-theta	1943	1849G>A	E617K
L05186	L05186	600758	GEN-174	Homo sapiens focal adhesion kinase mRNA, complete cds	2564	2550C>T	S
L05485	L05485	178635	GEN-MJL	Surfactant, pulmonary-associated protein D	921	918T>C	S
L05597	L05597	None	GEN-4EV	Serotonin 5-HT receptors	824	600T>C	S
L05597	L05597	None	GEN-4EV	Serotonin 5-HT receptors	1010	786*787insA [H262Q;26 ATAAATTC 2*263insl AT KFI]	
EDNRB	L06623	131244	GEN-19S	Endothelin Receptor Type B	88	(-146)A>G	5

EDNRB	L06623	131244	GEN-19S	Endothelin Receptor Type B	332	99C>T	S
EDNRB	L06623	131244	GEN-19S	Endothelin Receptor Type B	1064	831G>A	S
EDNRB	L06623	131244	GEN-19S	Endothelin Receptor Type B	1064	831G>A	S
EHHADH	L07077	261515	GEN-1DF	Human enoyl-CoA: hydratase 3-hydroxyacyl-CoA dehydrogenase (EHHADH) mRNA, complete cds with repeats	1225	1218G>A	S
EHHADH	L07077	261515	GEN-1DF	Human enoyl-CoA: hydratase 3-hydroxyacyl-CoA dehydrogenase (EHHADH) mRNA, complete cds with repeats	1823	1816C>A	P606T
ADD1	L07261	102680	GEN-1DJ	Human alpha adducin mRNA, partial cds including alternate exons A and B	1852	1853C>G	3
TGFBR3	L07594	600742	GEN-1EA	Human transforming growth factor-beta type III receptor (TGF-beta) mRNA, complete cds	3966	3618G>C	3
L07861	L07861	176977	GEN-D0	Protein kinase C, delta	445	387G>A	S
L07861	L07861	176977	GEN-D0	Protein kinase C, delta	1835	1777G>A	V593M
CCKBR	L08112	118445	GEN-1FL	Cholecystokinin (CCKb)	456	456G>A	S
FACL1	L09229	152425	GEN-1GI	Human long-chain acyl-coenzyme A synthetase (FACL1) mRNA, complete cds	3026	2953G>A	3
FACL1	L09229	152425	GEN-1GI	Human long-chain acyl-coenzyme A synthetase (FACL1) mRNA, complete cds	3083	3010G>A	3
L10819	L10819	171150	GEN-LVD	Homo sapiens aryl sulfotransferase mRNA, complete cds	191	153C>T	S
L10819	L10819	171150	GEN-LVD	Homo sapiens aryl sulfotransferase mRNA, complete cds	200	162G>A	S

L10819	L10819	171150	GEN- LVD	complete cds Homo sapiens aryl sulfotransferase mRNA, 230	192T>C	S
L10819	L10819	171150	GEN- LVD	complete cds Homo sapiens aryl sulfotransferase mRNA, 242	204G>A	S
L10819	L10819	171150	GEN- LVD	complete cds Homo sapiens aryl sulfotransferase mRNA, 295	257C>T	A86V
L10819	L10819	171150	GEN- LVD	complete cds Homo sapiens aryl sulfotransferase mRNA, 330	292G>A	D98N
L10819	L10819	171150	GEN- LVD	complete cds Homo sapiens aryl sulfotransferase mRNA, 338	300G>A	S
L10819	L10819	171150	GEN- LVD	complete cds Homo sapiens aryl sulfotransferase mRNA, 638	600C>G	S
L10819	L10819	171150	GEN- LVD	complete cds Homo sapiens aryl sulfotransferase mRNA, 676	638A>G	H213R
L10819	L10819	171150	GEN- LVD	complete cds Homo sapiens aryl sulfotransferase mRNA, 940	902G>A	3
L10819	L10819	171150	GEN- LVD	complete cds Homo sapiens aryl sulfotransferase mRNA, 1011	973T>C	3
C4BPB	L11244	120831	GEN- 1K2	complete cds Human (clone A12) C4b- binding protein beta-chain mRNA, complete cds 538	204G>A	S
C4BPB	L11244	120831	GEN- 1K2	complete cds Human (clone A12) C4b- binding protein beta-chain mRNA, complete cds 796	462C>T	S
C4BPB	L11244	120831	GEN- 1K2	complete cds Human (clone A12) C4b- binding protein beta-chain mRNA, complete cds 958	624C>A	S
L11669	L11669	102680	GEN- 1KW	complete cds Human tetracycline transporter-like protein mRNA, complete cds 544	424G>A	A142T
L11669	L11669	102680	GEN-	complete cds Human tetracycline transporter-like protein mRNA, complete cds 980	860C>T	S287L

L11669	L11669	102680	1KW	transporter-like protein mRNA, complete cds	1173G>A	S
	GEN-1KW			Human tetracycline transporter-like protein mRNA, complete cds		
MDCR	L13385	601545	GEN-1O6	Homo sapiens(clone 71) Miller-Dieker lissencephaly protein (LIS1) mRNA, complete cds	1250C>T	3
MDCR	L13385	601545	GEN-1O6	Homo sapiens(clone 71) Miller-Dieker lissencephaly protein (LIS1) mRNA, complete cds	1651C>T	3
MDCR	L13385	601545	GEN-1O6	Homo sapiens(clone 71) Miller-Dieker lissencephaly protein (LIS1) mRNA, complete cds	1700C>T	3
MDCR	L13385	601545	GEN-1O6	Homo sapiens(clone 71) Miller-Dieker lissencephaly protein (LIS1) mRNA, complete cds	2745G>T	3
MDCR	L13385	601545	GEN-1O6	Homo sapiens(clone 71) Miller-Dieker lissencephaly protein (LIS1) mRNA, complete cds	4372G>A	3
L13436	L13436	108961	GEN-2Q	guanylate cyclase	1411T>A	3
L13436	L13436	108961	GEN-2Q	guanylate cyclase	1647C>G	3
L13436	L13436	108961	GEN-2Q	guanylate cyclase	1651G>C	3
L13436	L13436	108961	GEN-2Q	guanylate cyclase	1678C>G	3
L13436	L13436	108961	GEN-2Q	guanylate cyclase	2223C>T	3
L13436	L13436	108961	GEN-2Q	guanylate cyclase	2445C>T	3
L13977	L13977	176785	GEN-1PX	Human 2009 prollycarboxypeptidase mRNA, complete cds	1980T>C	3
BF	L15702	138470	GEN-1UA	Human complement factor B mRNA, complete cds	95A>G	Q32R
PRKCI	L18964	300094	GEN-21N	Human protein kinase C iota isoform (PRKCI) mRNA, complete cds	309T>G	S
L19182	L19182	602867	GEN-	Human MAC25 mRNA, 297	284G>A	R95K

L19956	L19956	600641	21Z GEN- LVE	complete cds Human aryl 243 sulfotransferase mRNA,	105A>G	S
L19956	L19956	600641	GEN- LVE	complete cds Human aryl 284 sulfotransferase mRNA,	146C>T	S49F
L20463	L20463	600445	GEN-M	complete cds G-protein coupled 1671 adenosine A3 receptor	1380A>G	3
VLDLR	L20470	192977	GEN- 23D	Human very low density 336 lipoprotein receptor mRNA,	(-56)C>T	5
VLDLR	L20470	192977	GEN- 23D	complete cds Human very low density 3566 lipoprotein receptor mRNA,	3175T>C	3
L22214	L22214	102775	GEN-2S	complete cds Adenosine A1 receptor 557 (ADORA1)	147G>C	S
L22214	L22214	102775	GEN-2S	Adenosine A1 receptor 2622 (ADORA1)	2212G>A	3
L22473	L22473	600040	GEN- L9D	Human Bax alpha mRNA, 552 complete cds	552G>A	S
SLC6A3	L24178	126455	GEN-283	Homo sapiens dopamine 1917 transporter mRNA,	1898C>T	3
L24470	L24470	600563	GEN-O	complete cds PROSTAGLANDIN F 1422 RECEPTOR	1185T>C	3
L24470	L24470	600563	GEN-O	PROSTAGLANDIN F 1490 RECEPTOR	1253C>T	3
L24470	L24470	600563	GEN-O	PROSTAGLANDIN F 1517 RECEPTOR	1280A>G	3
L24470	L24470	600563	GEN-O	PROSTAGLANDIN F 2244 RECEPTOR	2007A>G	3
L24470	L24470	600563	GEN-O	PROSTAGLANDIN F 2299 RECEPTOR	2062A>G	3
L26232	L26232	172425	GEN- 2AK	Human phospholipid 906 transfer protein mRNA,	819C>T	S
L26232	L26232	172425	GEN- 2AK	complete cds Human phospholipid 1547 transfer protein mRNA,	1460C>A	T487K
L27624	L27624	600033	GEN- Homo sapiens tissue factor 213	complete cds	175C>G	Q59E

L27624	L27624	600033	2C8	pathway inhibitor-2 mRNA, complete cds	219C>A	S
L27624	L27624	600033	GEN-2C8	Homo sapiens tissue factor 257 pathway inhibitor-2 mRNA, complete cds	257G>T	C86F
L27624	L27624	600033	GEN-2C8	Homo sapiens tissue factor 295 pathway inhibitor-2 mRNA, complete cds	396G>A	S
L27624	L27624	600033	GEN-2C8	Homo sapiens tissue factor 434 pathway inhibitor-2 mRNA, complete cds	398A>T	N133I
L27624	L27624	600033	GEN-2C8	Homo sapiens tissue factor 436 pathway inhibitor-2 mRNA, complete cds	763G>A	3
L27624	L27624	600033	GEN-2C8	Homo sapiens tissue factor 801 pathway inhibitor-2 mRNA, complete cds	847C>A	3
PTGER2	L28175	601586	GEN-7C	Prostaglandin E receptor 2 547 (subtype EP2), 53kD	159C>T	S
PTGER2	L28175	601586	GEN-7C	Prostaglandin E receptor 2 611 (subtype EP2), 53kD	223G>A	V75M
PTGER2	L28175	601586	GEN-7C	Prostaglandin E receptor 2 1725 (subtype EP2), 53kD	1337A>G	Q446R
L31773	L31773	104220	GEN-4DD	Adrenergic receptor alpha 171 1b	171C>T	S
L31773	L31773	104220	GEN-4DD	Adrenergic receptor alpha 534 1b	534C>T	S
L31773	L31773	104220	GEN-4DD	Adrenergic receptor alpha 549 1b	549G>A	S
L34357	L34357	600576	GEN-KV3	Homo sapiens GATA-4 1996 mRNA, complete cds	1756T>C	3
L34357	L34357	600576	GEN-KV3	Homo sapiens GATA-4 2133 mRNA, complete cds	1893C>G	3
L36566	L36566	601970	GEN-2N5	Human helodermin-1397 preferring VIP receptor (VIP2/PACAP receptor) mRNA, complete cds	1235A>G	H412R
L36566	L36566	601970	GEN-	Human helodermin-1440	1278A>C	S

2N5			preferring VIP receptor (VIP2/PACAP receptor) mRNA, complete cds	1092	1083C>T	S
NRAMP2	L37347	600523	Human integral membrane protein (Nramp2) mRNA, partial	2968	2947C>T	3
L38969	L38969	None	Homo sapiens thrombospondin 3 (THBS3) gene, complete cds			
L41147	L41147	601109	Serotonin 5-HT receptors 5-HT6	287	(-181)C>T	5
L41147	L41147	601109	Serotonin 5-HT receptors 5-HT6	1718	1251C>T	S
L48513	L48513	602447	Homo sapiens paraoxonase 2 (PON2) mRNA, complete cds	460	443C>G	A148G
L48513	L48513	602447	Homo sapiens paraoxonase 2 (PON2) mRNA, complete cds	598	581G>A	G194E
L48513	L48513	602447	Homo sapiens paraoxonase 2 (PON2) mRNA, complete cds	949	932G>C	C311S
L78207	L78207	600509	Cell surface receptor for sulfonylureas on pancreatic b cells Insulin receptor	4019	3981A>G	S
M10051	M10051	147670	Insulin receptor	2757	2619G>A	S
M10051	M10051	147670	Insulin receptor	4391	4253G>A	3
M11146	M11146	134770	Human ferritin H chain mRNA, complete cds	193	116C>T	S39F
M11146	M11146	134770	Human ferritin H chain mRNA, complete cds	326	249T>G	S
M11146	M11146	134770	Human ferritin H chain mRNA, complete cds	628	551A>T	F
M11146	M11146	134770	Human ferritin H chain mRNA, complete cds	630	553G>A	3
M11146	M11146	134770	Human ferritin H chain mRNA, complete cds	652	575G>A	3
FTL	M11147	134790	Human ferritin L chain mRNA, complete cds	180	29C>A	S10Y
FTL	M11147	134790	Human ferritin L chain	240	89C>A	T30N

FTL	M11147	134790	GEN-1JZ	mRNA, complete cds	163C>T	S
				Human ferritin L chain 314		
FTL	M11147	134790	GEN-1JZ	mRNA, complete cds	189C>A	F
				Human ferritin L chain 340		
FTL	M11147	134790	GEN-1JZ	mRNA, complete cds	224G>A	G75D
				Human ferritin L chain 375		
FTL	M11147	134790	GEN-1JZ	mRNA, complete cds	600T>G	3
				Human ferritin L chain 751		
TF	M12530	190000	GEN-1MK	mRNA, complete cds	624G>A	S
				Human transferrin mRNA, 654		
TF	M12530	190000	GEN-1MK	complete cds	738C>G	C246W
				Human transferrin mRNA, 768		
TF	M12530	190000	GEN-1MK	complete cds	1417G>T	V473F
				Human transferrin mRNA, 1447		
TF	M12530	190000	GEN-1MK	complete cds	1572G>C	S
				Human transferrin mRNA, 1602		
TF	M12530	190000	GEN-1MK	complete cds	1602C>T	S
				Human transferrin mRNA, 1632		
TF	M12530	190000	GEN-1MK	complete cds	1765C>T	P589S
				Human transferrin mRNA, 1795		
M12674	M12674	133430	GEN-7Z	complete cds	975C>G	S
				Estrogen receptor 1267		
M12783	M12783	190040	GEN-QF	Human c-sis/platelet-derived growth factor 2 (SIS/PDGF2) mRNA, complete cds	804T>C	3
				Human c-sis/platelet-derived growth factor 2 (SIS/PDGF2) mRNA, complete cds		
M12783	M12783	190040	GEN-QF	Human c-sis/platelet-derived growth factor 2 (SIS/PDGF2) mRNA, complete cds	1056T>C	3
				Human c-sis/platelet-derived growth factor 2 (SIS/PDGF2) mRNA, complete cds		
M12783	M12783	190040	GEN-QF	Human c-sis/platelet-derived growth factor 2 (SIS/PDGF2) mRNA, complete cds	1158G>A	3
				Human c-sis/platelet-derived growth factor 2 (SIS/PDGF2) mRNA, complete cds		
M13686	M13686	178630	GEN-1P1	Human pulmonary surfactant-associated protein mRNA, complete cds, clone MPSAP-6A	56C>T	A19V
				Human pulmonary surfactant-associated protein mRNA, complete cds		
M13686	M13686	178630	GEN-1P1	Human pulmonary surfactant-associated protein mRNA, complete cds	253T>C	C85R
				Human pulmonary surfactant-associated protein mRNA, complete cds		

M13686	M13686	178630	GEN-1P1	cds, clone MPSAP-6A Human pulmonary surfactant-associated protein mRNA, complete	370	282G>A	S
M13686	M13686	178630	GEN-1P1	cds, clone MPSAP-6A Human pulmonary surfactant-associated protein mRNA, complete	430	342T>C	S
M13686	M13686	178630	GEN-1P1	cds, clone MPSAP-6A Human pulmonary surfactant-associated protein mRNA, complete	694	606C>T	S
M13686	M13686	178630	GEN-1P1	cds, clone MPSAP-6A Human pulmonary surfactant-associated protein mRNA, complete	736	648C>T	S
M13686	M13686	178630	GEN-1P1	cds, clone MPSAP-6A Human pulmonary surfactant-associated protein mRNA, complete	883	795C>G	3
C1NH	M13690	106100	GEN-1P6	Human plasma protease (C1) inhibitor mRNA, complete cds	1475	1438G>A	V480M
C1NH	M13690	106100	GEN-1P6	Human plasma protease (C1) inhibitor mRNA, complete cds	1595	1558C>T	3
C1NH	M13690	106100	GEN-1P6	Human plasma protease (C1) inhibitor mRNA, complete cds	1714	1677A>C	3
ALAD	M13928	125270	GEN-1Q2	Human delta-aminolevulinate dehydratase mRNA, complete cds	234	168T>C	S
ALAD	M13928	125270	GEN-1Q2	Human delta-aminolevulinate dehydratase mRNA, complete cds	480	414C>T	S
ALAD	M13928	125270	GEN-1Q2	Human delta-aminolevulinate dehydratase mRNA, complete cds	784	718C>T	R240W

BCL2	M13994	151430	GEN-1Q9	complete cds Human B-cell leukemia/lymphoma 2 (bcl-2) proto-oncogene mRNA encoding bcl-2-alpha protein, complete cds	1744	286G>A	A96T
BCL2	M13994	151430	GEN-1Q9	Human B-cell leukemia/lymphoma 2 (bcl-2) proto-oncogene mRNA encoding bcl-2-alpha protein, complete cds	1786	328G>C	G110R
BCL2	M13994	151430	GEN-1Q9	Human B-cell leukemia/lymphoma 2 (bcl-2) proto-oncogene mRNA encoding bcl-2-alpha protein, complete cds	2959	1501A>G	3
UROD	M14016	176100	GEN-1QM	Human uroporphyrinogen decarboxylase mRNA, complete cds	248	230C>T	P77L
UROD	M14016	176100	GEN-1QM	Human uroporphyrinogen decarboxylase mRNA, complete cds	850	832G>T	F
C1R	M14058	216950	GEN-1QJ	Human complement C1r mRNA, complete cds	1519	1456C>T	R486C
M14113	M14113	306700	GEN-5T	Factor VIII	8899	8728G>A	3
ARG1	M14502	207800	GEN-1RE	Human liver arginase mRNA, complete cds	800	744C>T	S
M14539	M14539	134570	GEN-QP	Human factor XIII subunit a mRNA, 3 end	1781	1781C>T	P594L
M14539	M14539	134570	GEN-QP	Human factor XIII subunit a mRNA, 3 end	2041	2041C>G	Q681E
M14539	M14539	134570	GEN-QP	Human factor XIII subunit a mRNA, 3 end	2412	2412C>T	3
M14539	M14539	134570	GEN-QP	Human factor XIII subunit a mRNA, 3 end	2446	2446G>A	3
M14539	M14539	134570	GEN-QP	Human factor XIII subunit a mRNA, 3 end	3282	3282G>T	3
M14565	M14565	118485	GEN-30	Cytochrome P450, subfamily XIA (cholesterol side chain cleavage)	947	903G>C	M301I
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	466	(-1122)C>G	5

M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	565	(-1023)G>A	5
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	1182	(-406)C>T	5
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	1221	(-367)C>T	5
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	1326	(-262)G>A	5
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	1541	(-47)C>T	5
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	1633	46A>G	R16G
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	1633	46A>G	R16G
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	1666	79C>G	Q27E
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	1666	79C>G	Q27E
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	1666	79C>G	Q27E
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	1687	100G>A	V34M
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	1839	252G>A	S
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	2110	523C>A	S
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	2640	1053G>C	S
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	2826	1239G>A	S
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	2862	1275C>G	3
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	2864	1277C>A	3
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	2865	1278C>A	3
M15169	M15169	109690	GEN-T	Beta2 Adrenergic Receptor	3371	1784A>T	3
PCNA	M15796	176740	GEN-	Human cyclin protein gene,	1063	945C>G	3
			1UE	complete cds			
DAF	M15799	125240	GEN-	Human complement	1160	1160A>C	3
			1UD	decay-accelerating factor			
				(DAF) mRNA; 3' end			
M15856	M15856	238600	GEN-33	Lipoprotein lipase	136	(-39)T>C	5
M15856	M15856	238600	GEN-33	Lipoprotein lipase	280	106G>A	D36N
M15856	M15856	238600	GEN-33	Lipoprotein lipase	438	264T>A	F
M15856	M15856	238600	GEN-33	Lipoprotein lipase	447	273G>A	F
M15856	M15856	238600	GEN-33	Lipoprotein lipase	474	300C>A	F
M15856	M15856	238600	GEN-33	Lipoprotein lipase	480	306A>C	R102S
M15856	M15856	238600	GEN-33	Lipoprotein lipase	511	337T>C	W113R
M15856	M15856	238600	GEN-33	Lipoprotein lipase	571	397C>T	F
M15856	M15856	238600	GEN-33	Lipoprotein lipase	680	506G>A	G169E
M15856	M15856	238600	GEN-33	Lipoprotein lipase	722	548A>G	D183G
M15856	M15856	238600	GEN-33	Lipoprotein lipase	770	596C>G	S199C
M15856	M15856	238600	GEN-33	Lipoprotein lipase	781	607G>A	A203T

M15856	M15856	238600	GEN-33	Lipoprotein lipase	795	621C>G	D207E
M15856	M15856	238600	GEN-33	Lipoprotein lipase	818	644G>A	G215E
M15856	M15856	238600	GEN-33	Lipoprotein lipase	836	662T>C	I221T
M15856	M15856	238600	GEN-33	Lipoprotein lipase	839	665G>A	G222E
M15856	M15856	238600	GEN-33	Lipoprotein lipase	843	669C>T	S
M15856	M15856	238600	GEN-33	Lipoprotein lipase	867	693C>G	D231E
M15856	M15856	238600	GEN-33	Lipoprotein lipase	875	701C>T	P234L
M15856	M15856	238600	GEN-33	Lipoprotein lipase	916	742delG	F
M15856	M15856	238600	GEN-33	Lipoprotein lipase	983	809G>A	R270H
M15856	M15856	238600	GEN-33	Lipoprotein lipase	985	811T>A	S271T
M15856	M15856	238600	GEN-33	Lipoprotein lipase	1003	829G>A	D277N
M15856	M15856	238600	GEN-33	Lipoprotein lipase	1127	953A>G	N318S
M15856	M15856	238600	GEN-33	Lipoprotein lipase	1255	1081G>A	A361T
M15856	M15856	238600	GEN-33	Lipoprotein lipase	1348	1174C>G	L392V
M15856	M15856	238600	GEN-33	Lipoprotein lipase	1401	1227G>A	F
M15856	M15856	238600	GEN-33	Lipoprotein lipase	1508	1334G>A	C445Y
M15856	M15856	238600	GEN-33	Lipoprotein lipase	1553	1379C>T	A460V
M15856	M15856	238600	GEN-33	Lipoprotein lipase	1595	1421C>G	F
M15856	M15856	238600	GEN-33	Lipoprotein lipase	1611	1437G>A	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	1973	1799T>C	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	2428	2254T>A	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	2743	2569T>C	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	2851	2677A>G	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	2851	2677A>G	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	2958	2784G>A	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	3017	2843T>C	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	3272	3098T>C	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	3272	3098T>C	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	3343	3169T>C	3
M15856	M15856	238600	GEN-33	Lipoprotein lipase	3447	3273C>T	3
M16006	M16006	173360	GEN-34	Tissue Plasminogen activator inhibitor, type I	124	49G>A	V171
M16006	M16006	173360	GEN-34	Tissue Plasminogen activator inhibitor, type I	411	336T>C	S
M16006	M16006	173360	GEN-34	Tissue Plasminogen activator inhibitor, type I	1645	1570T>C	3

M16006	M16006	173360	GEN-34	Tissue Plasminogen activator inhibitor, type I	1974	189T>C	3
M16006	M16006	173360	GEN-34	Tissue Plasminogen activator inhibitor, type I	2006	193T>G	3
M16405	M16405	None	GEN-4ES	Muscarinic receptor, CHRM4	2138	1338C>T	S
M16405	M16405	None	GEN-4ES	Muscarinic receptor, CHRM4	2409	1609G>A	3
M16538	M16538	139390	GEN-1Y8	Human signal-transducing guanine nucleotide-binding regulatory (G) protein beta subunit mRNA, complete cds	867	720C>T	S
M16538	M16538	139390	GEN-1Y8	Human signal-transducing guanine nucleotide-binding regulatory (G) protein beta subunit mRNA, complete cds	1270	1123G>T	3
M16538	M16538	139390	GEN-1Y8	Human signal-transducing guanine nucleotide-binding regulatory (G) protein beta subunit mRNA, complete cds	1388	1241C>T	3
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	422	293A>G	D98G
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	557	428G>A	G143D
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	564	435-436TT>AG>A	F146V
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	568	439C>T	F
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	596	467A>G	Y156C
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	941	812C>T	T271M
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	961	832A>C	T278P
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	978	849G>C	E283D
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1201	1072T>A	L358I
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1306	1177G>A	G393R
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1382	1253G>T	G418V
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1549	1420T>G	F474V
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1564	1435G>T	F
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1703	1574A>T	E525V

M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1756	1627C>T	R543C
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1828	1699G>A	A567T
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	1828	1699G>A	A567T
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	2127	1998A>G	3
M16541	M16541	177400	GEN-35	Butyrylcholinesterase	2127	1998A>G	3
M16660	M16660	140571	GEN-1YC	Human 90-kDa heat-shock protein gene, cDNA, complete cds	825	741G>A	S
M16801	M16801	600983	GEN-36	Mineralocorticoid receptor (aldosterone receptor)	175	(-42)C>G	5
M16801	M16801	600983	GEN-36	Mineralocorticoid receptor (aldosterone receptor)	754	538A>G	I180V
M16801	M16801	600983	GEN-36	Mineralocorticoid receptor (aldosterone receptor)	938	722C>T	A241V
M16801	M16801	600983	GEN-36	Mineralocorticoid receptor (aldosterone receptor)	1221	1005delC	F
M16801	M16801	600983	GEN-36	Mineralocorticoid receptor (aldosterone receptor)	1591	1375delT	F
M16801	M16801	600983	GEN-36	Mineralocorticoid receptor (aldosterone receptor)	1713	1497C>T	S
M16801	M16801	600983	GEN-36	Mineralocorticoid receptor (aldosterone receptor)	1825	1609C>T	F
M16801	M16801	600983	GEN-36	Mineralocorticoid receptor (aldosterone receptor)	2438	2222T>G	V741G
M16801	M16801	600983	GEN-36	Mineralocorticoid receptor (aldosterone receptor)	2730	2514G>A	S
M16801	M16801	600983	GEN-36	Mineralocorticoid receptor (aldosterone receptor)	5243	5027T>A	3
M16801	M16801	600983	GEN-36	Mineralocorticoid receptor (aldosterone receptor)	5645	5429G>A	3
M16827	M16827	201450	GEN-EI	Acyl-Coenzyme A 1956 dehydrogenase, C-4 to C-12 straight chain	1956	1938T>C	3
F5	M16967	227400	GEN-1Z8	Human coagulation factor V mRNA, complete cds	2391	2301G>A	S
F5	M16967	227400	GEN-1Z8	Human coagulation factor V mRNA, complete cds	2663	2573G>A	R858K
F5	M16967	227400	GEN-1Z8	Human coagulation factor V mRNA, complete cds	2684	2594G>A	R865H
F5	M16967	227400	GEN-1Z8	Human coagulation factor V mRNA, complete cds	5380	5290G>A	V1764M

C8B	M16973	120960	128 GEN-1ZA	V mRNA, complete cds Human complement protein C8 beta subunit mRNA, complete cds	1860	1833C>T	3
M17262	M17262	176930	GEN-SM	Human prothrombin (F2) gene, complete cds, and Alu and KpnI repeats	511	480C>T	S
C8G	M17999	120930	GEN-20Y	Human complement component C8-gamma mRNA, complete cds	193	132T>G	S
M18112	M18112	173870	GEN-EK	ADP-ribosyltransferase (NAD+; poly (ADP-ribose) polymerase)	2424	2285T>C	V762A
M18112	M18112	173870	GEN-EK	ADP-ribosyltransferase (NAD+; poly (ADP-ribose) polymerase)	2679	2540G>T	R847L
M18182	M18182	173370	GEN-37	Tissue Plasminogen activator, tissue type (t-PA)	391	378G>A	S
M18182	M18182	173370	GEN-37	Tissue Plasminogen activator, tissue type (t-PA)	499	486C>T	S
M18182	M18182	173370	GEN-37	Tissue Plasminogen activator, tissue type (t-PA)	514	501C>T	S
M18182	M18182	173370	GEN-37	Tissue Plasminogen activator, tissue type (t-PA)	1822	1809G>A	3
M18182	M18182	173370	GEN-37	Tissue Plasminogen activator, tissue type (t-PA)	1977	1964A>G	3
M18182	M18182	173370	GEN-37	Tissue Plasminogen activator, tissue type (t-PA)	2161	2148G>C	3
M20132	M20132	313700	GEN-38	Androgen receptor (dihydrotestosterone receptor)	995	633G>A	S
M20132	M20132	313700	GEN-38	Androgen receptor (dihydrotestosterone receptor)	1385	1023T>C	S
M20132	M20132	313700	GEN-38	Androgen receptor (dihydrotestosterone receptor)	1786	1424G>A	G475E
M20137	M20137	147740	GEN-CCJ	Human interleukin 3 (IL-3) mRNA, complete cds, clone pcD-SR-alpha	132	79C>T	P27S
M20560	M20560	106490	GEN-39	Lipocortin III (Annexin III)	1057	1011C>T	3

M20560	M20560	106490	GEN-39	Lipocortin III (Annexin III)	1302	1256C>A	3
M20566	M20566	147880	GEN-3A	Interleukin 6A	3058	2621A>T	3
M21054	M21054	172410	GEN-3B	Phospholipase A-2 (PLA-2)	331	294G>A	S
				lung			
M21054	M21054	172410	GEN-3B	Phospholipase A-2 (PLA-2)	400	363C>A	D121E
				lung			
CYBA	M21186	233690	GEN-24I	Human neutrophil cytochrome b light chain p22 phagocyte b- cytochrome mRNA, complete cds	242	214C>T	H72Y
				Human neutrophil	549		
CYBA	M21186	233690	GEN-24I	cytochrome b light chain p22 phagocyte b- cytochrome mRNA, complete cds	549	521C>T	A174V
				Human neutrophil	640		
CYBA	M21186	233690	GEN-24I	cytochrome b light chain p22 phagocyte b- cytochrome mRNA, complete cds	640	612A>G	3
				Human neutrophil	665		
CYBA	M21186	233690	GEN-24I	cytochrome b light chain p22 phagocyte b- cytochrome mRNA, complete cds	665	637C>T	3
				Human neutrophil	665		
M21616	M21616	173410	GEN-R1	Human platelet-derived growth factor (PDGF) receptor mRNA, complete cds	4312	4126C>T	3
				Human platelet-derived	5171		
M21616	M21616	173410	GEN-R1	growth factor (PDGF) receptor mRNA, complete cds	5171	4985C>A	3
				Human platelet-derived	5295		
M21616	M21616	173410	GEN-R1	growth factor (PDGF) receptor mRNA, complete cds	5295	5109A>G	3
				Human platelet-derived	5295		
PLA2G2A	M22430	172411	GEN-25V	Human RASFA PLA2 mRNA, complete cds	116	(-20)G>T	5
PLA2G2A	M22430	172411	GEN-	Human RASFA PLA2	231	96G>C	S

PLA2G2A	M22430	172411	25V GEN-	mRNA, complete cds			
PLA2G2A	M22430	172411	25V GEN-	Human RAS-F-A PLA2	267	132C>T	S
PLA2G2A	M22430	172411	25V GEN-	mRNA, complete cds			
PLA2G2A	M22430	172411	25V GEN-	Human RAS-F-A PLA2	267	132C>T	S
PLA2G2A	M22430	172411	25V GEN-	mRNA, complete cds			
PLA2G2A	M22430	172411	25V GEN-	Human RAS-F-A PLA2	278	143-144GT>GT	S
PLA2G2A	M22430	172411	25V GEN-	mRNA, complete cds			
PLA2G2A	M22430	172411	25V GEN-	Human RAS-F-A PLA2	278	144GT>GT	F
PLA2G2A	M22430	172411	25V GEN-	mRNA, complete cds			
PLA2G2A	M22430	172411	25V GEN-	Human RAS-F-A PLA2	643	508C>T	3
PLA2G2A	M22430	172411	25V GEN-	mRNA, complete cds			
PLA2G2A	M22430	172411	25V GEN-	Human RAS-F-A PLA2	700	565G>C	3
M22613	M22613	227600	25V GEN-3C	mRNA, complete cds			
ATP2A2	M23114	108740	GEN-276	COAGULATION FACTOR	738	738C>T	S
				X PRECURSOR			
				Homo sapiens calcium-ATPase (HK1) mRNA, complete cds	2382	2219C>T	S740F
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	238	167A>T	K56M
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	238	167A>T	K56M
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	792	721G>A	G241R
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	792	721G>A	G241R
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	1126	1055C>T	P352L
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	1166	1095C>T	S
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	1295	1224G>A	S
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	1476	1405A>G	K469E
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	1476	1405A>G	K469E
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	1476	1405A>G	K469E
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	2043	1972C>T	3
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	2043	1972C>T	3

M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	2551	2480C>T	3
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	2681	2610G>A	3
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	2842	2771G>A	3
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	2842	2771G>A	3
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	2935	2864T>C	3
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	2938	2867G>A	3
M24283	M24283	147840	GEN-V	Intercellular adhesion molecule 1	2950	2879C>T	3
CD36	M24795	173510	GEN-28R	Human CD36 antigen mRNA, complete cds	79	(-132)C>A	5
CD36	M24795	173510	GEN-28R	Human CD36 antigen mRNA, complete cds	341	131T>G	L44R
CD36	M24795	173510	GEN-28R	Human CD36 antigen mRNA, complete cds	1851	1641A>G	3
M25813	M25813	None	GEN-2A0	Human unidentified gene complementary to P450c21 gene, partial cds	1357	1357G>A	V453I
M25813	M25813	None	GEN-2A0	Human unidentified gene complementary to P450c21 gene, partial cds	2082	2082C>G	I694M
M25813	M25813	None	GEN-2A0	Human unidentified gene complementary to P450c21 gene, partial cds	2502	2502G>A	3
M25813	M25813	None	GEN-2A0	Human unidentified gene complementary to P450c21 gene, partial cds	2626	2626A>G	3
M26383	M26383	146930	GEN-3E	Interleukin 8	259	185C>G	A62G
M26383	M26383	146930	GEN-3E	Interleukin 8	1237	1163A>T	3
M26383	M26383	146930	GEN-3E	Interleukin 8	1281	1207A>G	3
M26393	M26393	201470	GEN-EW	Acyl-Coenzyme A 1797 dehydrogenase, C-2 to C-3 short chain	1797	1765A>G	3
M27137	M27137	109715	GEN-5W	3beta hydroxysteroid dehydrogenase	1103	1100C>A	T367N

M27436	M27436	134390	GEN-R7	Human tissue factor gene, 1414 complete cds, with a Alu repetitive sequence in the 3 untranslated region	1315C>T	3
M27436	M27436	134390	GEN-R7	Human tissue factor gene, 1508 complete cds, with a Alu repetitive sequence in the 3 untranslated region	1409A>G	3
M27436	M27436	134390	GEN-R7	Human tissue factor gene, 1588 complete cds, with a Alu repetitive sequence in the 3 untranslated region	1489T>G	3
M27492	M27492	147810	GEN-3F	INTERLEUKIN 1 4686 RECEPTOR, TYPE I PRECURSOR	4604T>G	3
M27875	M27875	107680	GEN-2CK	Human apolipoprotein A-I 34 mRNA, complete cds	15G>C	S
M27875	M27875	107680	GEN-2CK	Human apolipoprotein A-I 202 mRNA, complete cds	183C>T	S
M27875	M27875	107680	GEN-2CK	Human apolipoprotein A-I 204 mRNA, complete cds	185T>G	L62W
M27875	M27875	107680	GEN-2CK	Human apolipoprotein A-I 255 mRNA, complete cds	236C>T	S79F
M27875	M27875	107680	GEN-2CK	Human apolipoprotein A-I 689 mRNA, complete cds	670C>T	S
M27875	M27875	107680	GEN-2CK	Human apolipoprotein A-I 824 mRNA, complete cds	805G>A	3
M28226	M28226	158105	GEN-R8	Human JE gene encoding 90 a monocyte secretory protein mRNA, complete cds	44C>G	A15G
M28226	M28226	158105	GEN-R8	Human JE gene encoding 151 a monocyte secretory protein mRNA, complete cds	105C>T	S
M28226	M28226	158105	GEN-R8	Human JE gene encoding 411 a monocyte secretory protein mRNA, complete cds	365T>C	3
M28614	M28614	107720	GEN-6Q	Apolipoprotein C-III 370	340C>G	3
M28614	M28614	107720	GEN-6Q	Apolipoprotein C-III 401	371T>G	3

M28614	M28614	107720	GEN-6Q	Apolipoprotein C-III	479	449T>A	3
CFTR	M28668	602421	GEN-2DF	Human cystic fibrosis mRNA, encoding a presumed transmembrane conductance regulator (CFTR)	2729	2597G>A	C866Y
CFTR	M28668	602421	GEN-2DF	Human cystic fibrosis mRNA, encoding a presumed transmembrane conductance regulator (CFTR)	5826	5694T>C	3
M29551	M29551	114106	GEN-F3	SERINE/THREONINE PROTEIN PHOSPHATASE 2B CATALYTIC SUBUNIT, BETA ISOFORM	936	820G>A	V274M
M29551	M29551	114106	GEN-F3	SERINE/THREONINE PROTEIN PHOSPHATASE 2B CATALYTIC SUBUNIT, BETA ISOFORM	2640	2524G>A	3
M29696	M29696	146661	GEN-3H	Interleukin 7 receptor	1088	1066G>A	V356I
M29882	M29882	107670	GEN-6R	Apolipoprotein A-II	26	17C>A	A6E
M29882	M29882	107670	GEN-6R	Apolipoprotein A-II	183	174G>A	S
M29882	M29882	107670	GEN-6R	Apolipoprotein A-II	192	183C>A	S
CETP	M30185	118470	GEN-2FK	Human cholesteryl ester transfer protein mRNA, complete cds	1283	1153G>C	V385L
CETP	M30185	118470	GEN-2FK	Human cholesteryl ester transfer protein mRNA, complete cds	1298	1168G>C	A390P
CETP	M30185	118470	GEN-2FK	Human cholesteryl ester transfer protein mRNA, complete cds	1394	1264A>G	I422V
CETP	M30185	118470	GEN-2FK	Human cholesteryl ester transfer protein mRNA, complete cds	1394	1264A>G	I422V
CETP	M30185	118470	GEN-2FK	Human cholesteryl ester transfer protein mRNA, complete cds	1506	1376A>G	D459G

CETP	M30185	118470	GEN-2FK	Human cholesteryl ester transfer protein mRNA, complete cds	1696	1566G>A	3
M30262	M30262	600295	GEN-WA	Human cardiolipin-atrial natriuretic factor (CDD-ANF) mRNA, complete cds	178	79C>T	P27S
M30262	M30262	600295	GEN-WA	Human cardiolipin-atrial natriuretic factor (CDD-ANF) mRNA, complete cds	203	104C>G	A35G
M30262	M30262	600295	GEN-WA	Human cardiolipin-atrial natriuretic factor (CDD-ANF) mRNA, complete cds	210	111G>T	S
M30262	M30262	600295	GEN-WA	Human cardiolipin-atrial natriuretic factor (CDD-ANF) mRNA, complete cds	327	228C>T	S
M30262	M30262	600295	GEN-WA	Human cardiolipin-atrial natriuretic factor (CDD-ANF) mRNA, complete cds	553	454T>C	F
M30262	M30262	600295	GEN-WA	Human cardiolipin-atrial natriuretic factor (CDD-ANF) mRNA, complete cds	626	527G>T	3
M30262	M30262	600295	GEN-WA	Human cardiolipin-atrial natriuretic factor (CDD-ANF) mRNA, complete cds	640	541T>C	3
M30773	M30773	114106	GEN-X	Calcineurin B type I	331	(-428)T>C	5
M30773	M30773	114106	GEN-X	Calcineurin B type I	1658	900C>A	3
M31145	M31145	146730	GEN-3J	Insulin-like growth factor binding protein 1 precursor	923	759A>G	I253M
M31145	M31145	146730	GEN-3J	Insulin-like growth factor binding protein 1 precursor	1048	884T>C	3
M31145	M31145	146730	GEN-3J	Insulin-like growth factor binding protein 1 precursor	1260	1096C>G	3
PRKAR2 B	M31158	176912	GEN-2GE	Human cAMP-dependent protein kinase subunit RII-beta mRNA, complete cds	2790	2624C>G	3
M31159	M31159	146732	GEN-2GD	Human growth hormone-dependent insulin-like growth factor-binding protein mRNA, complete cds	204	95G>C	G32A
M31159	M31159	146732	GEN-	Human growth hormone-cds	2178	2069A>T	3

2GD	M31328	M31328	139130	GEN-7G	dependent insulin-like growth factor-binding protein mRNA, complete cds	1049	1043G>A	3
	M32313	M32313	184753	GEN-5Y	Guanine nucleotide binding protein (G protein), beta polypeptide 3	1271	1241C>T	3
	M32313	M32313	184753	GEN-5Y	Steroid 5 alpha reductase 1	1344	1314G>A	3
	M32313	M32313	184753	GEN-5Y	Steroid 5 alpha reductase 1	1489	1459G>A	3
	M32313	M32313	184753	GEN-5Y	Steroid 5 alpha reductase 1	1780	1750T>C	3
	VEGF	M32977	192240	GEN-2JF	Human heparin-binding vascular endothelial growth factor (VEGF) mRNA, complete cds	50	(-7)C>T	5
	VEGF	M32977	192240	GEN-2JF	Human heparin-binding vascular endothelial growth factor (VEGF) mRNA, complete cds	92	36C>T	S
	M33336	M33336	188830	GEN-RC	Human cAMP-dependent protein kinase type I-alpha subunit (PRKAR1A) mRNA, complete cds	2440	2353T>G	3
	M33336	M33336	188830	GEN-RC	Human cAMP-dependent protein kinase type I-alpha subunit (PRKAR1A) mRNA, complete cds	2472	2385C>T	3
	M33336	M33336	188830	GEN-RC	Human cAMP-dependent protein kinase type I-alpha subunit (PRKAR1A) mRNA, complete cds	3005	2918T>C	3
	M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3 mRNA, complete cds	53	35T>C	V12A
	M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	149	131C>A	A44D
	M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	194	176T>C	L59P
	M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	364	346C>T	L116F
	M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	900	882T>C	S

M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	987	969G>T	E323D
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	1161	1143C>A	S
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	1161	1143C>A	S
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	1551	1533G>A	S
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	1551	1533G>A	S
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	1562	1544G>A	R515Q
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	1563	1545G>A	S
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	1563	1545G>A	S
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	2226	2208C>T	S
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	2426	2408G>C	3
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	3056	3038C>T	3
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	3098	3080A>G	3
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	3403	3385A>T	3
M35999	M35999	173470	GEN-Y	Leukocyte integrin beta-3	3927	3909C>T	3
PLCG2	M37238	600220	GEN-2O1	Phospholipase C gamma-2	449	297A>G	S
PLCG2	M37238	600220	GEN-2O1	Phospholipase C gamma-2	883	731A>G	H244R
PLCG2	M37238	600220	GEN-2O1	Phospholipase C gamma-2	922	770A>T	H257L
PLCG2	M37238	600220	GEN-2O1	Phospholipase C gamma-2	954	802C>T	R268W
PLCG2	M37238	600220	GEN-2O1	Phospholipase C gamma-2	1301	1149T>C	S
PLCG2	M37238	600220	GEN-2O1	Phospholipase C gamma-2	1649	1497T>C	S
PLCG2	M37238	600220	GEN-2O1	Phospholipase C gamma-2	2666	2514G>A	S
PLCG2	M37238	600220	GEN-2O1	Phospholipase C gamma-2	3245	3093C>T	S
PLCG2	M37238	600220	GEN-2O1	Phospholipase C gamma-2	3245	3093C>T	S
PLCG2	M37238	600220	GEN-2O1	Phospholipase C gamma-2	3436	3284G>A	G1095D
PLCG2	M37238	600220	GEN-2O1	Phospholipase C gamma-2	4207	4055C>G	3
PAM	M37721	170270	GEN-2OK	Human peptidylglycine alpha-amidating monooxygenase mRNA,	3183	2995T>A	3

PAM	M37721	170270	GEN-2OK	Human peptidylglycine alpha-amidating monooxygenase mRNA, complete cds	3530	3342A>G	3
M37825	M37825	165190	GEN-2OM	Human fibroblast growth factor-5 (FGF-5) mRNA, complete cds	787	648T>G	S
M54968	M54968	190070	GEN-35G	Human K-ras oncogene protein mRNA, complete cds	711	519T>C	S
M54968	M54968	190070	GEN-35G	Human K-ras oncogene protein mRNA, complete cds	936	744G>T	3
M54968	M54968	190070	GEN-35G	Human K-ras oncogene protein mRNA, complete cds	1270	1078T>C	3
M54968	M54968	190070	GEN-35G	Human K-ras oncogene protein mRNA, complete cds	3268	3076T>G	3
M54968	M54968	190070	GEN-35G	Human K-ras oncogene protein mRNA, complete cds	4529	4337A>C	3
M54968	M54968	190070	GEN-35G	Human K-ras oncogene protein mRNA, complete cds	4555	4363A>G	3
M54968	M54968	190070	GEN-35G	Human K-ras oncogene protein mRNA, complete cds	4672	4480A>C	3
M55040	M55040	100740	GEN-3Q	acetylcholinesterase	323	167C>T	P56L
M55040	M55040	100740	GEN-3Q	acetylcholinesterase	1154	998T>A	V333E
M55040	M55040	100740	GEN-3Q	acetylcholinesterase	1213	1057C>A	H353N
M55040	M55040	100740	GEN-3Q	acetylcholinesterase	1482	1326G>T	S
M55040	M55040	100740	GEN-3Q	acetylcholinesterase	1587	1431C>T	S
M55040	M55040	100740	GEN-3Q	acetylcholinesterase	1587	1431C>T	S
M55040	M55040	100740	GEN-3Q	acetylcholinesterase	1663	1507T>C	F503L
M55040	M55040	100740	GEN-3Q	Human 47-kD autosomal chronic granulomatous disease protein mRNA, complete cds	291	269G>A	R90H
NCF1	M55067	233700	GEN-35R				

NCF1	M55067	233700	GEN-35R	Human 47-kD autosomal chronic granulomatous disease protein mRNA, complete cds	367	345C>T	S
NCF1	M55067	233700	GEN-35R	Human 47-kD autosomal chronic granulomatous disease protein mRNA, complete cds	409	387G>A	S
NCF1	M55067	233700	GEN-35R	Human 47-kD autosomal chronic granulomatous disease protein mRNA, complete cds	518	496G>A	D166N
NCF1	M55067	233700	GEN-35R	Human 47-kD autosomal chronic granulomatous disease protein mRNA, complete cds	580	558G>A	S
NCF1	M55067	233700	GEN-35R	Human 47-kD autosomal chronic granulomatous disease protein mRNA, complete cds	847	825T>C	S
NCF1	M55067	233700	GEN-35R	Human 47-kD autosomal chronic granulomatous disease protein mRNA, complete cds	871	849G>A	S
NCF1	M55067	233700	GEN-35R	Human 47-kD autosomal chronic granulomatous disease protein mRNA, complete cds	930	908C>T	S303L
NCF1	M55067	233700	GEN-35R	Human 47-kD autosomal chronic granulomatous disease protein mRNA, complete cds	945	923C>T	A308V
NCF1	M55067	233700	GEN-35R	Human 47-kD autosomal chronic granulomatous disease protein mRNA, complete cds	958	936T>C	S
NCF1	M55067	233700	GEN-35R	Human 47-kD autosomal chronic granulomatous disease protein mRNA, complete cds	966	944C>T	S315L
NCF1	M55067	233700	GEN-35R	Human 47-kD autosomal chronic granulomatous disease protein mRNA, complete cds	1024	1002G>A	S

NCF1	M55067	233700	35R	chronic granulomatous disease protein mRNA, complete cds	1089	1067C>A	T356K
NCF1	M55067	233700	GEN-35R	Human 47-kD autosomal chronic granulomatous disease protein mRNA, complete cds	1098	1076C>T	S359F
NCF1	M55067	233700	GEN-35R	Human 47-kD autosomal chronic granulomatous disease protein mRNA, complete cds	1250	1228C>T	3
M55643	M55643	164011	GEN-RP	Human factor KBF1 mRNA, complete cds	1936	1755G>A	S
M57899	M57899	191740	GEN-38A	Human bilirubin UDP-glucuronosyltransferase isozyme 1 mRNA, complete cds	1828	1813C>T	3
M57899	M57899	191740	GEN-38A	Human bilirubin UDP-glucuronosyltransferase isozyme 1 mRNA, complete cds	1956	1941C>G	3
M57899	M57899	191740	GEN-38A	Human bilirubin UDP-glucuronosyltransferase isozyme 1 mRNA, complete cds	2057	2042C>G	3
MYH7	M58018	160760	GEN-38J	Homo sapiens beta-myosin heavy chain (MYH7) mRNA, complete cds	407	321T>G	D107E
MYH7	M58018	160760	GEN-38J	Homo sapiens beta-myosin heavy chain (MYH7) mRNA, complete cds	818	732C>T	S
MYH7	M58018	160760	GEN-38J	Homo sapiens beta-myosin heavy chain (MYH7) mRNA, complete cds	2132	2046C>G	S
MYH7	M58018	160760	GEN-38J	Homo sapiens beta-myosin heavy chain (MYH7) mRNA, complete cds	2837	2751T>C	S

MYH7	M58018	160760	GEN-38J	Homo sapiens beta-myosin heavy chain (MYH7) mRNA, complete cds	2913	2827T>C	S
MYH7	M58018	160760	GEN-38J	Homo sapiens beta-myosin heavy chain (MYH7) mRNA, complete cds	3300	3214G>T	D1072Y
MYH7	M58018	160760	GEN-38J	Homo sapiens beta-myosin heavy chain (MYH7) mRNA, complete cds	3456	3370T>G	S1124A
MYH7	M58018	160760	GEN-38J	Homo sapiens beta-myosin heavy chain (MYH7) mRNA, complete cds	5507	5421C>G	S
M58525	M58525	116790	GEN-3S	Catechol-O- methyltransferase	390	186T>C	S
M58525	M58525	116790	GEN-3S	Catechol-O- methyltransferase	390	186T>C	S
M58525	M58525	116790	GEN-3S	Catechol-O- methyltransferase	418	214G>T	A72S
M58525	M58525	116790	GEN-3S	Catechol-O- methyltransferase	423	219G>A	S
M58525	M58525	116790	GEN-3S	Catechol-O- methyltransferase	612	408C>G	S
M58525	M58525	116790	GEN-3S	Catechol-O- methyltransferase	676	472A>G	M158V
M58525	M58525	116790	GEN-3S	Catechol-O- methyltransferase	676	472A>G	M158V
M58525	M58525	116790	GEN-3S	Catechol-O- methyltransferase	813	609C>T	S
M58525	M58525	116790	GEN-3S	Catechol-O- methyltransferase	1031	827delC	F
M58525	M58525	116790	GEN-3S	Catechol-O- methyltransferase	1039	835C>A	3
M59305	M59305	108962	GEN-39P	Human atrial natriuretic peptide clearance receptor (ANP C-receptor) mRNA, complete cds	160	(-203)-(-199)delTTTTT	F
M59979	M59979	176805	GEN-Z	Cyclooxygenase 1 COX1	644	639C>A	S
M59979	M59979	176805	GEN-Z	Cyclooxygenase 1 COX1	1892	1887C>A	3
M59979	M59979	176805	GEN-Z	Cyclooxygenase 1 COX1	2030	2025G>A	3
M60335	M60335	192225	GEN-3U	Vascular cell adhesion molecule 1	1562	1463A>G	H488R

M60335	M60335	192225	GEN-3U	Vascular cell adhesion molecule 1	2178	2079C>T	S
M60335	M60335	192225	GEN-3U	Vascular cell adhesion molecule 1	2178	2079C>T	S
M60335	M60335	192225	GEN-3U	Vascular cell adhesion molecule 1	2196	2097T>C	S
M60335	M60335	192225	GEN-3U	Vascular cell adhesion molecule 1	2307	2208A>G	S
M60335	M60335	192225	GEN-3U	Vascular cell adhesion molecule 1	2321	2222T>C	3
FGF7	M60828	148180	GEN-3BE	Human keratinocyte growth factor mRNA, complete cds	323	(-123)G>C	5
FGF7	M60828	148180	GEN-3BE	Human keratinocyte growth factor mRNA, complete cds	1180	735T>C	3
FGF7	M60828	148180	GEN-3BE	Human keratinocyte growth factor mRNA, complete cds	1201	756A>G	3
FGF7	M60828	148180	GEN-3BE	Human keratinocyte growth factor mRNA, complete cds	1216	771A>G	3
FGF7	M60828	148180	GEN-3BE	Human keratinocyte growth factor mRNA, complete cds	1218	773G>C	3
FGF7	M60828	148180	GEN-3BE	Human keratinocyte growth factor mRNA, complete cds	1266	821A>C	3
FGF7	M60828	148180	GEN-3BE	Human keratinocyte growth factor mRNA, complete cds	1306	861C>T	3
FGF7	M60828	148180	GEN-3BE	Human keratinocyte growth factor mRNA, complete cds	1654	1209A>T	3
FGF7	M60828	148180	GEN-3BE	Human keratinocyte growth factor mRNA, complete cds	1657	1212T>C	3
FGF7	M60828	148180	GEN-3BE	Human keratinocyte growth factor mRNA, complete cds	1799	1354A>T	3
FGF7	M60828	148180	GEN-3BE	Human keratinocyte growth factor mRNA, complete cds	1801	1356C>T	3

FGF7	M60828	148180	3BE	growth factor mRNA, complete cds			
GEN-3BE				Human keratinocyte growth factor mRNA,	1867	1422A>G	3
FGF7	M60828	148180	3BE	complete cds			
GEN-3BE				Human keratinocyte growth factor mRNA,	1945	1500C>A	3
FGF7	M60828	148180	3BE	complete cds			
GEN-3BE				Human keratinocyte growth factor mRNA,	1973	1528G>A	3
FGF7	M60828	148180	3BE	complete cds			
GEN-3BE				Human keratinocyte growth factor mRNA,	2167	1722G>A	3
FGF7	M60828	148180	3BE	complete cds			
GEN-3BE				Human keratinocyte growth factor mRNA,	2186	1741A>G	3
FGF7	M60828	148180	3BE	complete cds			
GEN-3BE				Human keratinocyte growth factor mRNA,	2302	1857T>A	3
FGF7	M60828	148180	3BE	complete cds			
GEN-3BE				Human keratinocyte growth factor mRNA,	2328	1883G>A	3
IGFBP4	M62403	146733	3CJ	Human insulin-like growth factor binding protein 4 (IGFBP4) mRNA, complete cds	859	776G>A	S
IGFBP4	M62403	146733	3CJ	Human insulin-like growth factor binding protein 4 (IGFBP4) mRNA, complete cds	1403	1320G>T	3
IGFBP4	M62403	146733	3CJ	Human insulin-like growth factor binding protein 4 (IGFBP4) mRNA, complete cds	1443	1360G>A	3
IGFBP4	M62403	146733	3CJ	Human insulin-like growth factor binding protein 4 (IGFBP4) mRNA, complete cds	1446	1363G>A	3
IGFBP4	M62403	146733	3CJ	Human insulin-like growth factor binding protein 4 cds	1485	1402A>T	3

M62424	M62424	187930	GEN-3W	(IGFBP4) mRNA, complete cds	Coagulation factor II (thrombin) receptor	3210	2986C>T	3
M62424	M62424	187930	GEN-3W		Coagulation factor II (thrombin) receptor	3211	2987G>A	3
M62424	M62424	187930	GEN-3W		Coagulation factor II (thrombin) receptor	3247	3023T>C	3
M62782	M62782	146734	GEN-3CU		Homo sapiens insulin-like growth factor binding protein 5 (IGFBP-5) mRNA, complete cds	908	852C>T	3
APOH	M62839	138700	GEN-3CY		Human apolipoprotein H mRNA, complete cds	500	461G>A	R154H
APOH	M62839	138700	GEN-3CY		Human apolipoprotein H mRNA, complete cds	835	796G>T	V266L
APOH	M62839	138700	GEN-3CY		Human apolipoprotein H mRNA, complete cds	1098	1059T>C	3
M63012	M63012	168820	GEN-9F		Paraoxonase 1 mRNA, complete cds	172	163A>T	M55L
LRPAP1	M63959	104225	GEN-3EI		Human alpha-2-macroglobulin receptor-associated protein mRNA, complete cds	850	837G>A	S
LRPAP1	M63959	104225	GEN-3EI		Human alpha-2-macroglobulin receptor-associated protein mRNA, complete cds	1093	1080C>T	3
LRPAP1	M63959	104225	GEN-3EI		Human alpha-2-macroglobulin receptor-associated protein mRNA, complete cds	1175	1162G>A	3
LRPAP1	M63959	104225	GEN-3EI		Human alpha-2-macroglobulin receptor-associated protein mRNA, complete cds	1249	1236C>T	3
LRPAP1	M63959	104225	GEN-3EI		Human alpha-2-macroglobulin receptor-associated protein mRNA, complete cds	1249	1236C>T	3
LRPAP1	M63959	104225	GEN-3EI		Human alpha-2-macroglobulin receptor-associated protein mRNA, complete cds	1392	1379T>G	3

FGFR3	M64347	134934	GEN-3EX	Human novel growth factor receptor mRNA, 3 cds	3108	3108C>A	3
FGFR3	M64347	134934	GEN-3EX	Human novel growth factor receptor mRNA, 3 cds	3715	3715G>A	3
M64592	M64592	120420	GEN-3X	Granulocyte colony-stimulating factor	271	271T>G	Y91D
M64592	M64592	120420	GEN-3X	Granulocyte colony-stimulating factor	1533	1533C>T	S
M64710	M64710	None	GEN-KUW	Human C-type natriuretic peptide gene, complete cds	199	200C>G	3
M64710	M64710	None	GEN-KUW	Human C-type natriuretic peptide gene, complete cds	777	778G>A	3
M64710	M64710	None	GEN-KUW	Human C-type natriuretic peptide gene, complete cds	1215	1216A>G	3
M64799	M64799	None	GEN-4DN	Histamine receptor H2	398	398T>C	V133A
M64799	M64799	None	GEN-4DN	Histamine receptor H2	525	525A>T	K175N
M64799	M64799	None	GEN-4DN	Histamine receptor H2	620	620A>G	K207R
M64799	M64799	None	GEN-4DN	Histamine receptor H2	649	649A>G	N217D
M64799	M64799	None	GEN-4DN	Histamine receptor H2	692	692A>G	K231R
M64799	M64799	None	GEN-4DN	Histamine receptor H2	802	802G>A	V268M
M65028	M65028	602372	GEN-3FM	Human hnRNP type A/B protein mRNA, complete cds	273	131C>G	P44R
M65028	M65028	602372	GEN-3FM	Human hnRNP type A/B protein mRNA, complete cds	595	453C>G	S
M65028	M65028	602372	GEN-3FM	Human hnRNP type A/B protein mRNA, complete cds	1255	1113A>G	3
PRKAR1	M65066	176911	GEN-	Human cAMP-dependent	1424	1424C>G	3

B		3FK	protein kinase regulatory subunit RI-beta mRNA, 3 end			
PRKAR1	M65066 176911	GEN-3FK	Human cAMP-dependent protein kinase regulatory subunit RI-beta mRNA, 3 end	1514	1514G>C	3
PRKAR1	M65066 176911	GEN-3FK	Human cAMP-dependent protein kinase regulatory subunit RI-beta mRNA, 3 end	1550	1550G>C	3
PRKAR1	M65066 176911	GEN-3FK	Human cAMP-dependent protein kinase regulatory subunit RI-beta mRNA, 3 end	1862	1862G>A	3
PRKAR1	M65066 176911	GEN-3FK	Human cAMP-dependent protein kinase regulatory subunit RI-beta mRNA, 3 end	2139	2139C>T	3
C5	M65134 120900	GEN-3FT	Human complement component C5 mRNA, 3end	1171	1171A>G	I391V
EDN2	M65199 131241	GEN-CBS	Endothelin 2	384	314C>T	A105V
EDN2	M65199 131241	GEN-CBS	Endothelin 2	997	927A>G	3
EDN2	M65199 131241	GEN-CBS	Endothelin 2	997	927A>G	3
M67439	M67439 126453	GEN-4EI	Dopamine Receptor D5	1500	1353T>A	S
M67439	M67439 126453	GEN-4EI	Dopamine Receptor D5	1512	1365G>A	F
M67439	M67439 126453	GEN-4EI	Dopamine Receptor D5	1566	1419G>A	S
M69013	M69013 139313	GEN-7L	Guanine nucleotide binding protein (G protein), alpha 11	957	771C>T	S
IGFBP6	M69054 146735	GEN-3J0	Human insulin-like growth factor binding protein 6 (IGFBP6) mRNA, complete mature peptide	751	751A>C	3
IGFBP6	M69054 146735	GEN-3J0	Human insulin-like growth factor binding protein 6 (IGFBP6) mRNA, complete	835	835A>C	3

IGFBP6	M69054	146735	GEN-3J0	mature peptide Human insulin-like growth factor binding protein 6 (IGFBP6) mRNA, complete	850	850G>A	3
M69226	M69226	309850	GEN-3Z	mature peptide Monoamine oxidase A	435	385A>C	S
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	936	886C>T	F
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	941	891T>G	S
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	941	891T>G	S
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	1076	1026A>T	S
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	1373	1323G>A	F
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	1460	1410C>T	S
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	1460	1410C>T	S
M69226	M69226	309850	GEN-3Z	Monoamine oxidase A	1609	1559A>G	K520R
SRD5A2	M74047	264600	GEN-CDC	Human steroid 5-alpha-reductase 2 (SRD5A2) mRNA, complete cds	2379	2352A>G	3
M74782	M74782	308385	GEN-64	Interleukin 3 receptor, alpha (low affinity)	1396	1250C>T	3
M77829	M77829	107776	GEN-3QJ	Human channel-like integral membrane protein (CHIP28) mRNA, complete cds	172	134C>T	A45V
M77829	M77829	107776	GEN-3QJ	Human channel-like integral membrane protein (CHIP28) mRNA, complete cds	1249	1211C>G	3
PAX6	M77844	106210	GEN-3QG	H.sapiens oculorhombin (aniridia) mRNA, complete cds	669	307C>T	F
M80646	M80646	274180	GEN-40	Thromboxane synthase	756	585G>C	S
M80646	M80646	274180	GEN-40	Thromboxane synthase	1240	1069C>G	L357V
M81181	M81181	182331	GEN-G4	ATPase, Na+/K+ transporting, beta 2 polypeptide	107	(-301)C>G	5
M81181	M81181	182331	GEN-G4	ATPase, Na+/K+ transporting, beta 2 polypeptide	1070	663C>A	S
M81181	M81181	182331	GEN-G4	ATPase, Na+/K+ transporting, beta 2 polypeptide	1974	1567C>A	3

M81181	M81181	182331	GEN-G4	transporting, beta 2 polypeptide ATPase, Na+/K+ transporting, beta 2	1957T>C	3
THBS2	M81339	188061	GEN-3VQ	Human thrombospondin mRNA	1685C>T	3
THBS2	M81339	188061	GEN-3VQ	Human thrombospondin mRNA	1921C>T	3
THBS2	M81339	188061	GEN-3VQ	Human thrombospondin mRNA	2035T>G	3
THBS2	M81339	188061	GEN-3VQ	Human thrombospondin mRNA	2332C>T	3
THBS2	M81339	188061	GEN-3VQ	Human thrombospondin mRNA	2562C>T	3
THBS2	M81339	188061	GEN-3VQ	Human thrombospondin mRNA	2656C>T	3
THBS2	M81339	188061	GEN-3VQ	Human thrombospondin mRNA	2730C>T	3
M81590	M81590	182131	GEN-3VZ	Serotonin 5-HT receptors 5-HT1D	129C>T	S
M81590	M81590	182131	GEN-3VZ	Serotonin 5-HT receptors 5-HT1D	371T>G	F124C
M81590	M81590	182131	GEN-3VZ	Serotonin 5-HT receptors 5-HT1D	861G>C	S
M81590	M81590	182131	GEN-3VZ	Serotonin 5-HT receptors 5-HT1D	1180G>A	3
M81757	M81757	603474	GEN-3W6	H.sapiens S19 ribosomal protein mRNA, complete cds	254A>T	N85I
M81757	M81757	603474	GEN-3W6	H.sapiens S19 ribosomal protein mRNA, complete cds	316G>A	A106T
M81757	M81757	603474	GEN-3W6	H.sapiens S19 ribosomal protein mRNA, complete cds	474G>A	3
M81768	M81768	107310	GEN-G6	Solute carrier family 9 (sodium/hydrogen exchanger)	2989G>A	3
M82962	M82962	600388	GEN-3XC	Human N-benzoyl-L-tyrosyl-p-amino-benzoic	2307T>G	3

M82962	M82962	600388	GEN-3XC	acid hydrolase alpha subunit (PPH alpha) mRNA, complete cds Human N-benzoyl-L-tyrosyl-p-amino-benzoic acid hydrolase alpha subunit (PPH alpha) mRNA, complete cds Nicotinic, Cholinergic receptor alpha 5	2419A>C	3
CHRNA5	M83712	118505	GEN-3YQ	Human 46	1192G>A	D398N
M84526	M84526	134350	GEN-3ZL	adipsin/complement factor D mRNA, complete cds Human 399	(-9)C>T	5
M84526	M84526	134350	GEN-3ZL	adipsin/complement factor D mRNA, complete cds Human 408	345C>A	S
M84526	M84526	134350	GEN-3ZL	adipsin/complement factor D mRNA, complete cds Human 859	354A>G	S
M84526	M84526	134350	GEN-3ZL	adipsin/complement factor D mRNA, complete cds Human 891	805C>T	3
M84526	M84526	134350	GEN-3ZL	adipsin/complement factor D mRNA, complete cds Human 891	837G>C	3
M84747	M84747	300007	GEN-45	Interleukin 9 receptor	1094G>A	R365H
M84755	M84755	162641	GEN-46	Neuropeptide Y1	1121A>C	K374T
TGFBR2	M85079	190182	GEN-3ZS	Human TGF-beta type II receptor mRNA, complete cds	1710A>C	3
YWHAZ	M86400	601288	GEN-40Y	Human phospholipase A2 mRNA, complete cds	1569T>A	3
YWHAZ	M86400	601288	GEN-40Y	Human phospholipase A2 mRNA, complete cds	2515C>G	3
YWHAZ	M86400	601288	GEN-40Y	Human phospholipase A2 mRNA, complete cds	2535A>C	3
YWHAZ	M86400	601288	GEN-40Y	Human phospholipase A2 mRNA, complete cds	2572A>C	3
YWHAZ	M86400	601288	GEN-40Y	Human phospholipase A2 mRNA, complete cds	2661C>T	3
YWHAZ	M86400	601288	GEN-40Y	Human phospholipase A2 mRNA, complete cds	2677A>C	3

GJB2	M86849	121011	GEN-41L	40Y	mRNA, complete cds	1948T>G	3
					Human connexin 26 (GJB2) mRNA		
GJB2	M86849	121011	GEN-41L		Human connexin 26 (GJB2) mRNA	2036A>G	3
OSBP	M86917	167040	GEN-425		Human oxysterol-binding protein (OSBP) mRNA, complete cds	(-265)T>G	5
OSBP	M86917	167040	GEN-425		Human oxysterol-binding protein (OSBP) mRNA, complete cds	322C>T	F
OSBP	M86917	167040	GEN-425		Human oxysterol-binding protein (OSBP) mRNA, complete cds	408C>T	S
OSBP	M86917	167040	GEN-425		Human oxysterol-binding protein (OSBP) mRNA, complete cds	454T>G	S152A
M87290	M87290	106165	GEN-19		Angiotensin receptor AT1	16T>C	S6P
M87290	M87290	106165	GEN-19		Angiotensin receptor AT1	133G>A	G45R
M87290	M87290	106165	GEN-19		Angiotensin receptor AT1	573T>C	S
M87290	M87290	106165	GEN-19		Angiotensin receptor AT1	573T>C	S
M87290	M87290	106165	GEN-19		Angiotensin receptor AT1	1062A>G	S
M87290	M87290	106165	GEN-19		Angiotensin receptor AT1	1062A>G	S
M87290	M87290	106165	GEN-19		Angiotensin receptor AT1	1150T>G	3
M87290	M87290	106165	GEN-19		Angiotensin receptor AT1	1166C>A	3
M87290	M87290	106165	GEN-19		Angiotensin receptor AT1	1166C>A	3
M87290	M87290	106165	GEN-19		Angiotensin receptor AT1	1166C>A	3
M87290	M87290	106165	GEN-19		Angiotensin receptor AT1	1173A>G	3
M87290	M87290	106165	GEN-19		Angiotensin receptor AT1	1397G>A	3
M87290	M87290	106165	GEN-19		Angiotensin receptor AT1	1517G>T	3
M87290	M87290	106165	GEN-19		Angiotensin receptor AT1	1605C>T	3
M87290	M87290	106165	GEN-19		Angiotensin receptor AT1	1636T>C	3
M87290	M87290	106165	GEN-19		Angiotensin receptor AT1	1878A>G	3
M90100	M90100	600262	GEN-1A		Cyclooxygenase 2 COX2	2062G>C	3
M90100	M90100	600262	GEN-1A		Cyclooxygenase 2 COX2	2089-2094ATATTA	3
						>ATATTA	
M90100	M90100	600262	GEN-1A		Cyclooxygenase 2 COX2	2089-	3

2094delATAT								TA
M90100	M90100	600262	GEN-1A	Cyclooxygenase 2	COX2	2230	2133A>G	3
M90100	M90100	600262	GEN-1A	Cyclooxygenase 2	COX2	2339	2242T>C	3
M90100	M90100	600262	GEN-1A	Cyclooxygenase 2	COX2	2409	2312G>A	3
M90100	M90100	600262	GEN-1A	Cyclooxygenase 2	COX2	2726	2629C>T	3
M90100	M90100	600262	GEN-1A	Cyclooxygenase 2	COX2	2983	2886C>T	3
M92269	M92269	114205	GEN-SV	Ca Channel alpha1c (alt. splice) L-Type		3846	3846C>T	S
M92269	M92269	114205	GEN-SV	Ca Channel alpha1c (alt. splice) L-Type		5505	5505G>A	S
M92269	M92269	114205	GEN-SV	Ca Channel alpha1c (alt. splice) L-Type		6582	6582A>G	S
M92269	M92269	114205	GEN-SV	Ca Channel alpha1c (alt. splice) L-Type		6613	6613G>C	G2205R
M92269	M92269	114205	GEN-SV	Ca Channel alpha1c (alt. splice) L-Type		6614	6614G>C	G2205A
PNLIP	M93285	246600	GEN-48N	Pancreatic lipase (PNLIP) (Dietary supplement)		646	646G>T	V216L
M95678	M95678	604114	GEN-4A6	Homo sapiens phospholipase C-beta-2 mRNA, complete cds		1346	1182T>C	S
M95678	M95678	604114	GEN-4A6	Homo sapiens phospholipase C-beta-2 mRNA, complete cds		3436	3272A>G	E1091G
M95678	M95678	604114	GEN-4A6	Homo sapiens phospholipase C-beta-2 mRNA, complete cds		4137	3973C>T	3
M95708	M95708	107271	GEN-SF	Homo sapiens Ly-6-like protein (CD59) mRNA, complete cds		497	435C>T	3
M96652	M96652	147851	GEN-65	Interleukin 5 receptor alpha		883	634T>G	S212A
GJA4	M96789	121012	GEN-4B1	Homo sapiens connexin 37 (GJA4) mRNA, complete cds		211	147G>A	S
GJA4	M96789	121012	GEN-4B1	Homo sapiens connexin 37 (GJA4) mRNA, complete cds		620	556G>A	V186M
GJA4	M96789	121012	GEN-4B1	Homo sapiens connexin 37 (GJA4) mRNA, complete cds		1019	955C>T	P319S

GJA4	M96789	121012	GEN-4B1	Homo sapiens connexin 37 (GJA4) mRNA, complete cds	1115A>G	3
GJA4	M96789	121012	GEN-4B1	Homo sapiens connexin 37 (GJA4) mRNA, complete cds	1159C>A	3
GJA4	M96789	121012	GEN-4B1	Homo sapiens connexin 37 (GJA4) mRNA, complete cds	1347G>A	3
GJA4	M96789	121012	GEN-4B1	Homo sapiens connexin 37 (GJA4) mRNA, complete cds	1413C>G	3
M98539	M98539	176803	GEN-SW	prostaglandin D2 synthase gene	158C>A	3
S70154	S70154	100678	GEN-GY	ACAT2	632A>G	K211R
S70154	S70154	100678	GEN-GY	ACAT2	783T>C	S
S70154	S70154	100678	GEN-GY	ACAT2	783T>C	S
S70154	S70154	100678	GEN-GY	ACAT2	819G>A	S
S70154	S70154	100678	GEN-GY	ACAT2	819G>A	S
S70154	S70154	100678	GEN-GY	ACAT2	1351T>G	3
S70154	S70154	100678	GEN-GY	ACAT2	1358-1362CTTIA>	3
S70154	S70154	100678	GEN-GY	ACAT2	CTTTA	
S70154	S70154	100678	GEN-GY	ACAT2	1358-1362delCTTT	F
S70154	S70154	100678	GEN-GY	ACAT2	1382C>A	3
S70154	S70154	100678	GEN-GY	ACAT2	1382C>A	3
ADCYAP	S83513	102980	GEN-3YA	pituitary adenylate cyclase activating polypeptide [human; mRNA, 1940 nt]	1520G>A	3
U00672	U00672	146933	GEN-4A	Interleukin 10 receptor	3316A>C	3
U00672	U00672	146933	GEN-4A	Interleukin 10 receptor	3463A>G	3
U00968	U00968	184756	GEN-UU	Human SREBP-1 mRNA, complete cds	3817G>A	3
U02031	U02031	600481	GEN-WD	Human sterol regulatory element binding protein-2 mRNA, complete cds	972G>A	S

U03642	U03642	None	GEN- KUU	Human G protein-coupled receptor APJ gene, complete cds	333	135A>C	S
U03642	U03642	None	GEN- KUU	Human G protein-coupled receptor APJ gene, complete cds	1096	898G>A	V300I
U03858	U03858	600007	GEN- MDM	Fms-related tyrosine kinase 3 ligand	683	600C>T	S
U03858	U03858	600007	GEN- MDM	Fms-related tyrosine kinase 3 ligand	1016	933T>C	3
U04270	U04270	152427	GEN-H6	Potassium channel subunit (h-erg)	1650	1467C>T	S
U04270	U04270	152427	GEN-H6	Potassium channel subunit (h-erg)	3888	3705A>C	3
HADHA	U04627	600890	GEN-155	Human 78 kDa gastrin- binding protein mRNA, complete cds	1507	1507G>A	V503M
CDC2L1	U04815	139380	GEN- 15P	Human protein kinase PITSLRE alpha 1 mRNA, complete cds	632	239C>T	S80L
CDC2L1	U04815	139380	GEN- 15P	Human protein kinase PITSLRE alpha 1 mRNA, complete cds	837	444G>C	S
CDC2L1	U04815	139380	GEN- 15P	Human protein kinase PITSLRE alpha 1 mRNA, complete cds	882	489C>T	S
CDC2L1	U04815	139380	GEN- 15P	Human protein kinase PITSLRE alpha 1 mRNA, complete cds	945	552T>C	S
CDC2L1	U04815	139380	GEN- 15P	Human protein kinase PITSLRE alpha 1 mRNA, complete cds	1119	726C>G	S
CDC2L1	U04815	139380	GEN- 15P	Human protein kinase PITSLRE alpha 1 mRNA, complete cds	1131	738C>T	S
CDC2L1	U04815	139380	GEN- 15P	Human protein kinase PITSLRE alpha 1 mRNA, complete cds	1134	741C>T	S
CDC2L1	U04815	139380	GEN- 15P	Human protein kinase PITSLRE alpha 1 mRNA, complete cds	1193	800T>A	L267Q

CDC2L1	U04815	139380	GEN-15P	Human protein kinase PITSLRE alpha 1 mRNA, complete cds	1266	873T>C	S
CDC2L1	U04815	139380	GEN-15P	Human protein kinase PITSLRE alpha 1 mRNA, complete cds	1314	921G>T	K307N
CDC2L1	U04815	139380	GEN-15P	Human protein kinase PITSLRE alpha 1 mRNA, complete cds	1692	1299C>A	D433E
CDC2L1	U04815	139380	GEN-15P	Human protein kinase PITSLRE alpha 1 mRNA, complete cds	1700	1307T>A	L436Q
CDC2L1	U04815	139380	GEN-15P	Human protein kinase PITSLRE alpha 1 mRNA, complete cds	1706	1313A>G	E438G
CDC2L1	U04815	139380	GEN-15P	Human protein kinase PITSLRE alpha 1 mRNA, complete cds	1776	1383C>T	S
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	38	15C>T	S
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	282	259A>T	S87C
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	350	327C>T	S
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	365	342T>C	S
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	464	441G>A	S
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	474	451A>G	M151V
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	532	509A>G	H170R
DDH1	U05598	600450	GEN-184	Human dihydrodiol dehydrogenase mRNA, complete cds	538	515T>A	L172Q

DDH1	U05598	600450	GEN-184	complete cds Human dihydrodiol dehydrogenase mRNA,	689	666T>C	S
DDH1	U05598	600450	GEN-184	complete cds Human dihydrodiol dehydrogenase mRNA,	806	783G>A	S
DDH1	U05598	600450	GEN-184	complete cds Human dihydrodiol dehydrogenase mRNA,	872	849G>T	S
DDH1	U05598	600450	GEN-184	complete cds Human dihydrodiol dehydrogenase mRNA,	952	929T>G	I310S
DDH1	U05598	600450	GEN-184	complete cds Human dihydrodiol dehydrogenase mRNA,	1020	997G>A	3
DDH1	U05598	600450	GEN-184	complete cds Human dihydrodiol dehydrogenase mRNA,	1035	1012G>A	3
DDH1	U05598	600450	GEN-184	complete cds Human dihydrodiol dehydrogenase mRNA,	1112	1089C>T	3
HSD17B3	U05659	264300	GEN-186	complete cds Human 17beta- hydroxysteroid dehydrogenase type 3 mRNA, complete cds	894	846G>C	S
U07225	U07225	600041	GEN-1DM	P2Y2 purinoceptor	2008	1763G>A	3
U09117	U09117	602142	GEN-1GC	Phospholipase C delta-1	333	239G>A	R80H
U09117	U09117	602142	GEN-1GC	Phospholipase C delta-1	460	366G>A	S
U09117	U09117	602142	GEN-1GC	Phospholipase C delta-1	1858	1764G>A	S
SLC18A3	U09210	600336	GEN-4F3	Human vesicular acetylcholine transporter mRNA, complete cds	838	396T>C	S
SLC18A3	U09210	600336	GEN-4F3	Human vesicular acetylcholine transporter mRNA, complete cds	1369	927A>G	S
SLC18A3	U09210	600336	GEN-	Human vesicular	1567	1125C>G	S

SLC18A3	U09210	600336	GEN-4F3	4F3	acetylcholine transporter mRNA, complete cds	2080	1638G>T	3
SLC18A3	U09210	600336	GEN-4F3	4F3	acetylcholine transporter mRNA, complete cds	2199	1757G>A	3
SLC18A3	U09210	600336	GEN-4F3	4F3	acetylcholine transporter mRNA, complete cds	2349	1907G>T	3
U09648	U09648	600650	GEN-1I	GEN-1I	acetylcholine transporter mRNA, complete cds	2556	2040G>A	3
U09648	U09648	600650	GEN-1I	GEN-1I	Palmitoyltransferase II	2675	2159G>A	3
U09648	U09648	600650	GEN-1I	GEN-1I	Palmitoyltransferase II	2792	2276G>A	3
U09648	U09648	600650	GEN-1I	GEN-1I	Palmitoyltransferase II	2825	2309G>A	3
U09759	U09759	602896	GEN-1HA	GEN-1HA	Palmitoyltransferase II	303	152A>G	N51S
U09759	U09759	602896	GEN-1HA	GEN-1HA	Human protein kinase (JNK2) mRNA, complete cds	1079	928A>G	I310V
U09759	U09759	602896	GEN-1HA	GEN-1HA	Human protein kinase (JNK2) mRNA, complete cds	1280	1129C>T	P377S
U09759	U09759	602896	GEN-1HA	GEN-1HA	Human protein kinase (JNK2) mRNA, complete cds	1559	1408C>T	3
U09806	U09806	None	GEN-4FZ	GEN-4FZ	Human protein kinase (JNK2) mRNA, complete cds	120	120T>C	S
U09806	U09806	None	GEN-4FZ	GEN-4FZ	methylene tetrahydrofolate reductase mRNA, partial cds	473	473G>A	R158Q
U09806	U09806	None	GEN-4FZ	GEN-4FZ	methylene tetrahydrofolate reductase mRNA, partial cds	550	550C>T	F

U09806	U09806	None	GEN-4FZ	reductase mRNA, partial cds Human 668 methylenetetrahydrofolate reductase mRNA, partial cds	668C>T	A223V
U09806	U09806	None	GEN-4FZ	Human 1059 methylenetetrahydrofolate reductase mRNA, partial cds	1059T>C	S
U09806	U09806	None	GEN-4FZ	Human 1289 methylenetetrahydrofolate reductase mRNA, partial cds	1289C>A	E430A
U09806	U09806	None	GEN-4FZ	Human 1308 methylenetetrahydrofolate reductase mRNA, partial cds	1308T>C	3
THPO	U11025	600044	GEN-1JW	Human megakaryocyte 76 growth and development factor (MGDF) mRNA, complete cds	41T>C	L14P
THPO	U11025	600044	GEN-1JW	Human megakaryocyte 172 growth and development factor (MGDF) mRNA, complete cds	137G>A	R46K
THPO	U11025	600044	GEN-1JW	Human megakaryocyte 382 growth and development factor (MGDF) mRNA, complete cds	347G>A	G116E
THPO	U11025	600044	GEN-1JW	Human megakaryocyte 674 growth and development factor (MGDF) mRNA, complete cds	639T>A	S
THPO	U11025	600044	GEN-1JW	Human megakaryocyte 1132 growth and development factor (MGDF) mRNA, complete cds	1097G>A	3
U12507	U12507	600681	GEN-1MD	Cardiac inward rectifier potassium channel (HH-IRK1)	13C>A	S

U12507	U12507	600681	GEN-1MD	Cardiac inward rectifier potassium channel (HHRK1)	1597	1272G>A	S
U12789	U12789	600234	GEN-4F	HMG CoA synthase (HSH1) mitochondrial	720	720T>A	H240Q
U13737	U13737	600636	GEN-1PC	Human cysteine protease CPP32 isoform alpha mRNA, complete cds	2356	2132A>C	3
U13737	U13737	600636	GEN-1PC	Human cysteine protease CPP32 isoform alpha mRNA, complete cds	2535	2311C>T	3
CTGF	U14750	121009	GEN-1S3	Human connective tissue growth factor mRNA, partial cds	1878	1878A>C	3
U16660	U16660	600696	GEN-1YD	Human peroxisomal enoyl-CoA hydratase-like protein (HPXEL) mRNA, complete cds	149	122A>C	E41A
U16660	U16660	600696	GEN-1YD	Human peroxisomal enoyl-CoA hydratase-like protein (HPXEL) mRNA, complete cds	402	375G>A	S
U16660	U16660	600696	GEN-1YD	Human peroxisomal enoyl-CoA hydratase-like protein (HPXEL) mRNA, complete cds	802	775C>G	P259A
U16660	U16660	600696	GEN-1YD	Human peroxisomal enoyl-CoA hydratase-like protein (HPXEL) mRNA, complete cds	1157	1130G>A	3
U16957	U16957	300034	GEN-1L	Angiotensin receptor AT2	263	123T>C	S
U16957	U16957	300034	GEN-1L	Angiotensin receptor AT2	883	743G>A	R248K
STAR	U17280	600617	GEN-208	Human steroidogenic acute regulatory protein (STAR) mRNA, complete cds	1439	1313C>T	3
NOS1	U17327	163731	GEN-209	Human neuronal nitric oxide synthase (NOS1) mRNA, complete cds	3391	2706C>T	S
U19487	U19487	176804	GEN-4I	PROSTAGLANDIN E2 RECEPTOR, EP2	85	(-72)A>G	5

U19487	U19487	176804	GEN-4I	PROSTAGLANDIN E2 RECEPTOR, EP2 SUBTYPE	231	75A>T	S
U19775	U19775	600289	GEN-22C	Human MAP kinase Mxi2 (MXI2) mRNA, complete cds	731	688G>A	D230N
U20157	U20157	601690	GEN-234	Human platelet-activating factor acetylhydrolase mRNA, complete cds	1297	1136T>C	V379A
U20180	U20180	147582	GEN-236	Human iron-regulatory protein 2 (IRP2) mRNA, partial cds	2583	2583C>T	S
U20536	U20536	601532	GEN-23K	Human cysteine protease Mch2 isoform alpha (Mch2) mRNA, complete cds	982	904C>T	3
U20536	U20536	601532	GEN-23K	Human cysteine protease Mch2 isoform alpha (Mch2) mRNA, complete cds	1117	1039G>A	3
U20536	U20536	601532	GEN-23K	Human cysteine protease Mch2 isoform alpha (Mch2) mRNA, complete cds	1322	1244T>C	3
U20536	U20536	601532	GEN-23K	Human cysteine protease Mch2 isoform alpha (Mch2) mRNA, complete cds	1363	1285T>C	3
U27325	U27325	188070	GEN-7N	Thromboxane A2 TP receptor, platelet and non-platelet	302	179G>T	R60L
U27325	U27325	188070	GEN-7N	Thromboxane A2 TP receptor, platelet and non-platelet	918	795T>C	S
U27467	U27467	601056	GEN-2BX	Human Bcl-2 related (Bfl-1) mRNA, complete cds	476	442T>C	F148L
U27467	U27467	601056	GEN-2BX	Human Bcl-2 related (Bfl-1) mRNA, complete cds	481	447A>G	S
U27467	U27467	601056	GEN-2BX	Human Bcl-2 related (Bfl-1) mRNA, complete cds	542	508C>G	L170V
U27467	U27467	601056	GEN-2BX	Human Bcl-2 related (Bfl-1) mRNA, complete cds	578	544C>T	3
U27467	U27467	601056	GEN-2BX	Human Bcl-2 related (Bfl-1) mRNA, complete cds	614	580T>C	3

U27467	U27467	601056	GEN-2BX	Human Bcl-2 related (Bfl-1) mRNA, complete cds	616	582G>A	3
U31628	U31628	601070	GEN-4J	Interleukin 15 receptor alpha chain	1250	1168G>T	3
U32324	U32324	600939	GEN-4K	interleukin 11 receptor alpha chain	1266	1205C>A	P402Q
U32324	U32324	600939	GEN-4K	interleukin 11 receptor alpha chain	1513	1452C>T	3
U32500	U32500	162642	GEN-1P	Neuropeptide Y2	407	159C>T	S
U32500	U32500	162642	GEN-1P	Neuropeptide Y2	833	585T>C	S
U32500	U32500	162642	GEN-1P	Neuropeptide Y2	833	585T>C	S
U32500	U32500	162642	GEN-1P	Neuropeptide Y2	1184	936T>C	S
U32500	U32500	162642	GEN-1P	Neuropeptide Y2	1184	936T>C	S
U32500	U32500	162642	GEN-1P	Neuropeptide Y2	1706	1458-1460TAT>TA	3
U32500	U32500	162642	GEN-1P	Neuropeptide Y2	1706	1458-1460delTAT	3
U32500	U32500	162642	GEN-1P	Neuropeptide Y2	2782	2534^2535ins CA	F
U32989	U32989	191070	GEN-2JH	Human tryptophan oxygenase (TDO) mRNA, complete cds	991	927G>A	S
U33052	U33052	602549	GEN-2JL	Human lipid-activated, protein kinase PRK2 mRNA, complete cds	34	25G>C	E9Q
U33052	U33052	602549	GEN-2JL	Human lipid-activated, protein kinase PRK2 mRNA, complete cds	430	421T>C	S
U33052	U33052	602549	GEN-2JL	Human lipid-activated, protein kinase PRK2 mRNA, complete cds	1112	1103T>G	F368C
GSS	U34683	601002	GEN-2LF	Human glutathione synthetase mRNA, complete cds	364	324G>A	S
FGF8	U36223	600483	GEN-2MX	Human fibroblast growth factor 8 (FGF-8) mRNA, complete cds	300	291T>C	S
FGF8	U36223	600483	GEN-2MX	Human fibroblast growth factor 8 (FGF-8) mRNA, complete cds	645	636G>C	S

FGF8	U36223	600483	GEN-2MX	Human fibroblast growth factor 8 (FGF-8) mRNA, complete cds	648	639A>G	S
U37448	U37448	601761	GEN-2OC	Human Mch3 isoform alpha (Mch3) mRNA, complete cds	736	693G>A	S
U37448	U37448	601761	GEN-2OC	Human Mch3 isoform alpha (Mch3) mRNA, complete cds	1285	1242T>C	3
U37448	U37448	601761	GEN-2OC	Human Mch3 isoform alpha (Mch3) mRNA, complete cds	1294	1251T>C	3
U37448	U37448	601761	GEN-2OC	Human Mch3 isoform alpha (Mch3) mRNA, complete cds	1580	1537A>T	3
U37448	U37448	601761	GEN-2OC	Human Mch3 isoform alpha (Mch3) mRNA, complete cds	1621	1578G>T	3
U37448	U37448	601761	GEN-2OC	Human Mch3 isoform alpha (Mch3) mRNA, complete cds	1715	1672G>A	3
U37448	U37448	601761	GEN-2OC	Human Mch3 isoform alpha (Mch3) mRNA, complete cds	1764	1721G>A	3
U38545	U38545	602382	GEN-2PB	Human ARF-activated phosphatidylcholine-specific phospholipase D1a (hPLD1) mRNA, complete cds	3100	3005T>G	F1002C
U40002	U40002	151750	GEN-2RH	Human hormone-sensitive lipase testicular isoform mRNA, complete cds	2076	1799C>A	P600H
U40038	U40038	600998	GEN-70	Guanine nucleotide binding protein (G protein), q polypeptide	825	783C>T	S
U40038	U40038	600998	GEN-70	Guanine nucleotide binding protein (G protein), q polypeptide	878	836T>C	L279P
U40038	U40038	600998	GEN-70	Guanine nucleotide binding protein (G protein), q polypeptide	1029	987G>A	S

U40038	U40038	600998	GEN-70	polypeptide Guanine nucleotide binding protein (G protein), q	1051	1009A>G	I337V
U40038	U40038	600998	GEN-70	polypeptide Guanine nucleotide binding protein (G protein), q	1068	1026T>A	S
U40038	U40038	600998	GEN-70	polypeptide Guanine nucleotide binding protein (G protein), q	1093	1051T>C	S
U40347	U40347	600950	GEN- 2RK	Human serotonin N- acetyltransferase mRNA, complete cds	382	148G>A	E50K
U40396	U40396	602691	GEN-6W	Steroid receptor coactivator (SRC-1)	285	229A>C	K77Q
U40396	U40396	602691	GEN-6W	Steroid receptor coactivator (SRC-1)	314	258A>T	K86N
U40396	U40396	602691	GEN-6W	Steroid receptor coactivator (SRC-1)	336	280C>T	P94S
U40396	U40396	602691	GEN-6W	Steroid receptor coactivator (SRC-1)	688	632C>T	T211I
U40396	U40396	602691	GEN-6W	Steroid receptor coactivator (SRC-1)	970	914C>A	A305E
U40396	U40396	602691	GEN-6W	Steroid receptor coactivator (SRC-1)	1511	1455G>A	S
U40396	U40396	602691	GEN-6W	Steroid receptor coactivator (SRC-1)	2377	2321C>T	T774M
U40396	U40396	602691	GEN-6W	Steroid receptor coactivator (SRC-1)	2730	2674C>T	P892S
U40583	U40583	118511	GEN-4O	Nicotinic, Cholinergic receptor alpha 7	661	654T>C	S
U40583	U40583	118511	GEN-4O	Nicotinic, Cholinergic receptor alpha 7	697	690A>G	S
U40583	U40583	118511	GEN-4O	Nicotinic, Cholinergic receptor alpha 7	940	933G>A	S
U40583	U40583	118511	GEN-4O	Nicotinic, Cholinergic receptor alpha 7	1276	1269T>C	S
U40583	U40583	118511	GEN-4O	Nicotinic, Cholinergic receptor alpha 7	1790	1783A>T	3
U40583	U40583	118511	GEN-4O	Nicotinic, Cholinergic receptor alpha 7	1792	1785T>A	3

U43142	U43142	601528	GEN-2UM	Human vascular endothelial growth factor related protein VRP mRNA, complete cds	1499	1128C>T	S
U45448	U45448	600845	GEN-4FI	Human P2x1 receptor mRNA, complete cds	1424	1228A>G	3
U45448	U45448	600845	GEN-4FI	Human P2x1 receptor mRNA, complete cds	1604	1408C>G	3
U45448	U45448	600845	GEN-4FI	Human P2x1 receptor mRNA, complete cds	1719	1523G>A	3
U45448	U45448	600845	GEN-4FI	Human P2x1 receptor mRNA, complete cds	1827	1631G>A	3
U45448	U45448	600845	GEN-4FI	Human P2x1 receptor mRNA, complete cds	2286	2090G>A	3
U48730	U48730	601511	GEN-JA	Transcription Factor Stat5b	494	484T>C	S
U48730	U48730	601511	GEN-JA	Transcription Factor Stat5b	496	486A>G	S
U48730	U48730	601511	GEN-JA	Transcription Factor Stat5b	499	489A>G	S
U48730	U48730	601511	GEN-JA	Transcription Factor Stat5b	502	492G>A	S
U48730	U48730	601511	GEN-JA	Transcription Factor Stat5b	570	560G>C	G187A
U48730	U48730	601511	GEN-JA	Transcription Factor Stat5b	573	563C>A	P188Q
U48730	U48730	601511	GEN-JA	Transcription Factor Stat5b	1003	993G>A	S
U48730	U48730	601511	GEN-JA	Transcription Factor Stat5b	1063	1053T>C	S
U48730	U48730	601511	GEN-JA	Transcription Factor Stat5b	1066	1056G>A	S
U48730	U48730	601511	GEN-JA	Transcription Factor Stat5b	1105	1095C>T	S
U48730	U48730	601511	GEN-JA	Transcription Factor Stat5b	1159	1149C>T	S
U48730	U48730	601511	GEN-JA	Transcription Factor Stat5b	1969	1959C>T	S
U49516	U49516	312861	GEN-1Q	Serotonin 5-HT receptors 5-HT2C	2915	2187A>C	3
U49516	U49516	312861	GEN-1Q	Serotonin 5-HT receptors 5-HT2C	2947	2219A>G	3
U50929	U50929	602888	GEN-JF	Methionine synthetase (aka homocysteine methyltransferase)	2017	1991A>G	3
U50929	U50929	602888	GEN-JF	Methionine synthetase (aka homocysteine methyltransferase)	2418	2392A>T	3
U51478	U51478	601867	GEN-31Z	Human sodium/potassium-transporting ATPase beta-3 subunit mRNA, complete	1099	1071G>C	3

U51478	U51478	601867	GEN-31Z	Human sodium/potassium-transporting ATPase beta-3 subunit mRNA, complete cds	1121	1093T>C	3
U51478	U51478	601867	GEN-31Z	Human sodium/potassium-transporting ATPase beta-3 subunit mRNA, complete cds	1133	1105G>T	3
U56390	U56390	602234	GEN-36X	Human cysteine protease ICE-LAP6 mRNA, complete cds	411	408C>T	S
U56976	U56976	171891	GEN-379	Human calmodulin dependent phosphodiesterase PDE1B1 mRNA, complete cds	1510	1476C>T	S
DES	U59167	125660	GEN-39F	Human desmin mRNA, complete cds	140	60C>G	S
DES	U59167	125660	GEN-39F	Human desmin mRNA, complete cds	905	825T>C	S
DES	U59167	125660	GEN-39F	Human desmin mRNA, complete cds	1091	1011C>G	S
DES	U59167	125660	GEN-39F	Human desmin mRNA, complete cds	1181	1101G>A	S
DES	U59167	125660	GEN-39F	Human desmin mRNA, complete cds	2176	2096C>A	3
U60519	U60519	601762	GEN-3AZ	Human apoptotic cysteine protease Mch4 (Mch4) mRNA, complete cds	304	157G>A	E53K
U60519	U60519	601762	GEN-3AZ	Human apoptotic cysteine protease Mch4 (Mch4) mRNA, complete cds	324	177A>G	S
CHRNA2	U62431	118502	GEN-4EN	Nicotinic, Cholinergic receptor alpha 2	2296	1742C>G	3
CHRNA2	U62431	118502	GEN-4EN	Nicotinic, Cholinergic receptor alpha 2	2387	1833C>T	3
CHRNA2	U62431	118502	GEN-4EN	Nicotinic, Cholinergic receptor alpha 2	2504	1950G>T	3
CHRNA2	U62431	118502	GEN-4EN	Nicotinic, Cholinergic receptor alpha 2	2538	1984G>A	3

U62433	U62433	118504	GEN-4P	Nicotinic, Cholinergic receptor alpha 4	870	639C>T	S
U62433	U62433	118504	GEN-4P	Nicotinic, Cholinergic receptor alpha 4	870	639C>T	S
U62433	U62433	118504	GEN-4P	Nicotinic, Cholinergic receptor alpha 4	909	678C>T	S
U62433	U62433	118504	GEN-4P	Nicotinic, Cholinergic receptor alpha 4	909	678C>T	S
U62433	U62433	118504	GEN-4P	Nicotinic, Cholinergic receptor alpha 4	1440	1209T>G	S
U62433	U62433	118504	GEN-4P	Nicotinic, Cholinergic receptor alpha 4	1440	1209T>G	S
U62433	U62433	118504	GEN-4P	Nicotinic, Cholinergic receptor alpha 4	1458	1227C>T	S
U62433	U62433	118504	GEN-4P	Nicotinic, Cholinergic receptor alpha 4	1584	1353G>A	S
U62433	U62433	118504	GEN-4P	Nicotinic, Cholinergic receptor alpha 4	1781	1550C>T	S517L
U62433	U62433	118504	GEN-4P	Nicotinic, Cholinergic receptor alpha 4	1860	1629C>T	S
U62433	U62433	118504	GEN-4P	Nicotinic, Cholinergic receptor alpha 4	1860	1629C>T	S
U62433	U62433	118504	GEN-4P	Nicotinic, Cholinergic receptor alpha 4	1890	1659G>A	S
U62433	U62433	118504	GEN-4P	Nicotinic, Cholinergic receptor alpha 4	1890	1659G>A	S
U62768	U62768	151300	GEN-3CR	Human oxytocinase splice variant 1 mRNA, complete	3356	3295G>C	3
U62768	U62768	151300	GEN-3CR	Human oxytocinase splice variant 1 mRNA, complete	3547	3486C>T	3
U70136	U70136	600044	GEN-4R	Thrombopoietin	4138	4105G>T	A1369S
U70136	U70136	600044	GEN-4R	Thrombopoietin	4141	4108T>A	F1370I
U70867	U70867	601460	GEN-4S	prostaglandin transporter hPGT	2706	2615T>G	3
U70867	U70867	601460	GEN-4S	prostaglandin transporter hPGT	2839	2748T>A	3
U70867	U70867	601460	GEN-4S	prostaglandin transporter hPGT	2908	2817A>G	3
U70867	U70867	601460	GEN-4S	prostaglandin transporter hPGT	3171	3080A>G	3

U70867	U70867	601460	GEN-4S	prostaglandin transporter hPGT	3171	3080A>G	3
U70867	U70867	601460	GEN-4S	prostaglandin transporter hPGT	3253	3162A>G	3
U70867	U70867	601460	GEN-4S	prostaglandin transporter hPGT	3255	3164A>G	3
U70867	U70867	601460	GEN-4S	prostaglandin transporter hPGT	3594	3503T>A	3
U71321	U71321	602623	GEN-2TW	Human FK506-binding protein FKBP51 mRNA, complete cds	1248	1095C>T	S
U71321	U71321	602623	GEN-2TW	Human FK506-binding protein FKBP51 mRNA, complete cds	1425	1272G>A	S
U73338	U73338	156570	GEN-69	Methionine Synthase	1158	764G>A	C255Y
U73338	U73338	156570	GEN-69	Methionine Synthase	5095	4701G>A	3
U73338	U73338	156570	GEN-69	Methionine Synthase	6750	6356G>A	3
U78294	U78294	603697	GEN-3QZ	Homo sapiens 15S-2449 lipoxigenase mRNA, complete cds	2449	2378A>G	3
U79269	U79269	123829	GEN-K7	Cyclin-Dependent Protein Kinase	1281	972A>T	3
U81375	U81375	602193	GEN-3VO	Human placental equilibrative nucleoside transporter 1 (hENT1) mRNA, complete cds	1989	1811G>A	3
U81375	U81375	602193	GEN-3VO	Human placental equilibrative nucleoside transporter 1 (hENT1) mRNA, complete cds	1996	1818C>T	3
U81375	U81375	602193	GEN-3VO	Human placental equilibrative nucleoside transporter 1 (hENT1) mRNA, complete cds	2045	1867T>C	3
U82812	U82812	602592	GEN-3X7	Human scavenger receptor cysteine rich Sp alpha mRNA, complete cds	1280	1220T>A	3
U96781	U96781	108730	GEN-MQL	ATPase, Ca++ transporting, cardiac muscle, fast twitch 1	3007	3007G>A	3

HBA1	V00493	141800	GEN-TK	Human messenger RNA 198 for alpha globin	161C>T	A54V
HBA1	V00493	141800	GEN-TK	Human messenger RNA 244 for alpha globin	207C>A	N69K
HBA1	V00493	141800	GEN-TK	Human messenger RNA 307 for alpha globin	270C>A	H90Q
HBA1	V00493	141800	GEN-TK	Human messenger RNA 314 for alpha globin	277C>T	R93W
HBA1	V00493	141800	GEN-TK	Human messenger RNA 326 for alpha globin	289G>T	V97F
HBA1	V00493	141800	GEN-TK	Human messenger RNA 393 for alpha globin	356C>A	T119N
HBA1	V00493	141800	GEN-TK	Human messenger RNA 399 for alpha globin	362C>G	A121G
HBA1	V00493	141800	GEN-TK	Human messenger RNA 418 for alpha globin	381C>A	D127E
HBA1	V00493	141800	GEN-TK	Human messenger RNA 481 for alpha globin	444A>G	3
V00497	V00497	141900	GEN-P1	Human messenger RNA 59 for beta-globin	9C>T	S
V00497	V00497	141900	GEN-P1	Human messenger RNA 257 for beta-globin	207C>A	S
V00497	V00497	141900	GEN-P1	Human messenger RNA 284 for beta-globin	234C>A	H78Q
V00497	V00497	141900	GEN-P1	Human messenger RNA 304 for beta-globin	254C>A	T85N
V00497	V00497	141900	GEN-P1	Human messenger RNA 370 for beta-globin	320T>C	L107P
V00497	V00497	141900	GEN-P1	Human messenger RNA 385 for beta-globin	335T>G	V112G
V00497	V00497	141900	GEN-P1	Human messenger RNA 529 for beta-globin	479T>G	3
V00497	V00497	141900	GEN-P1	Human messenger RNA 537 for beta-globin	487T>G	3
V00519	V00519	139250	GEN-4U	Growth hormone 1 299	259C>A	P87T
V00519	V00519	139250	GEN-4U	Growth hormone 1 524	484G>T	G162W
X00568	X00568	207750	GEN-6Z	Apolipoprotein C-II 70	70C>A	Q24K
X01060	X01060	190010	GEN-6C	Transferrin receptor (p90, 687 CD71)	424A>G	S142G
X01060	X01060	190010	GEN-6C	Transferrin receptor (p90, 2823 CD71)	2560delT	F

X01060	X01060	190010	GEN-6C	Transferrin receptor (p90, 3766 CD71)	3503T>G	3
X01060	X01060	190010	GEN-6C	Transferrin receptor (p90, 4122 CD71)	3859A>C	3
X01060	X01060	190010	GEN-6C	Transferrin receptor (p90, 4147 CD71)	3884G>A	3
X01060	X01060	190010	GEN-6C	Transferrin receptor (p90, 4247 CD71)	3984T>C	3
X01060	X01060	190010	GEN-6C	Transferrin receptor (p90, 4309 CD71)	4046T>A	3
X01060	X01060	190010	GEN-6C	Transferrin receptor (p90, 4381 CD71)	4118A>G	3
X01060	X01060	190010	GEN-6C	Transferrin receptor (p90, 4547 CD71)	4284G>A	3
X01060	X01060	190010	GEN-6C	Transferrin receptor (p90, 4619 CD71)	4356T>G	3
X01060	X01060	190010	GEN-6C	Transferrin receptor (p90, 4726 CD71)	4463A>T	3
X01060	X01060	190010	GEN-6C	Transferrin receptor (p90, 4766 CD71)	4503C>T	3
X01586	X01586	147680	GEN-PC	Interleukin 2 332	225T>G	H75Q
X01586	X01586	147680	GEN-PC	Interleukin 2 563	456G>A	S
X02317	X02317	147450	GEN-KM	Superoxide dismutase 1 614 (Cu/Zn)	550A>C	3
X02415	X02415	134850	GEN-MJ0	Human gene for fibrinogen 1000 gamma chain	949G>A	D317N
X02469	X02469	191170	GEN-PF	Human mRNA for p53 350 cellular tumor antigen	215C>G	P72R
X02469	X02469	191170	GEN-PF	Human mRNA for p53 953 cellular tumor antigen	818G>A	R273H
X02750	X02750	176860	GEN-4Z	Anticoagulant Protein C 1600 (inactivator of coagulation factors Va and VIIIa)	1503G>C	3
NRAS	X02751	164790	GEN-XG	Human N-ras mRNA and flanking regions 221	(-506)A>G	5
NRAS	X02751	164790	GEN-XG	Human N-ras mRNA and flanking regions 390	(-337)C>A	5
X02812	X02812	190180	GEN-XR	Human mRNA for 870 transforming growth factor-beta (TGF-beta)	29C>T	P10L
X02812	X02812	190180	GEN-XR	Human mRNA for 979	138C>G	I46M

X02812	X02812	190180	GEN-XR	transforming growth factor-beta (TGF-beta) Human mRNA for	1632	791C>T	T264I
X02812	X02812	190180	GEN-XR	transforming growth factor-beta (TGF-beta) Human mRNA for	1807	966C>T	S
X02812	X02812	190180	GEN-XR	transforming growth factor-beta (TGF-beta) Human mRNA for	1930	1089G>A	S
X02812	X02812	190180	GEN-XR	transforming growth factor-beta (TGF-beta) Human mRNA for	1942	1101C>T	S
X02812	X02812	190180	GEN-XR	transforming growth factor-beta (TGF-beta) Human mRNA for	2013	1172G>A	S391N
X03172	X03172	192340	GEN-ZM	transforming growth factor-beta (TGF-beta) Human mRNA for	379	356T>G	V119G
X03438	X03438	138970	GEN-PM	vasopressin precursor Human mRNA for	586	555G>A	S
X03438	X03438	138970	GEN-PM	granulocyte colony-stimulating factor (G-CSF) Human mRNA for	1235	1204C>T	3
X03635	X03635	133430	GEN-50	granulocyte colony-stimulating factor (G-CSF) estrogen receptors	390	30T>C	S
X03635	X03635	133430	GEN-50	estrogen receptors	390	30T>C	S
X03635	X03635	133430	GEN-50	estrogen receptors	424	64G>C	E22Q
X03635	X03635	133430	GEN-50	estrogen receptors	617	257C>T	A86V
X03635	X03635	133430	GEN-50	estrogen receptors	621	261G>C	S
X03635	X03635	133430	GEN-50	estrogen receptors	829	469C>T	F
X03635	X03635	133430	GEN-50	estrogen receptors	1335	975C>G	S
X03635	X03635	133430	GEN-50	estrogen receptors	1335	975C>G	S
X03635	X03635	133430	GEN-50	estrogen receptors	1451	1091T>A	V364E
X03635	X03635	133430	GEN-50	estrogen receptors	1674	1314G>A	M438I
X03635	X03635	133430	GEN-50	estrogen receptors	2142	1782A>G	S
X03635	X03635	133430	GEN-50	estrogen receptors	2354	1994A>G	3
X03635	X03635	133430	GEN-50	estrogen receptors	2550	2190A>C	3
X03635	X03635	133430	GEN-50	estrogen receptors	2733	2373C>G	3

X03635	X03635	133430	GEN-50	estrogen receptors	3181	2821T>C	3
X03635	X03635	133430	GEN-50	estrogen receptors	3338	2978C>T	3
X03635	X03635	133430	GEN-50	estrogen receptors	3652	3292-3294CCT>CC	3
X03635	X03635	133430	GEN-50	estrogen receptors	3652	T	3
X03635	X03635	133430	GEN-50	estrogen receptors	3896	3292-3294delCCT	3
X03635	X03635	133430	GEN-50	estrogen receptors	4378	3536C>A	3
X03635	X03635	133430	GEN-50	estrogen receptors	6287	4018T>C	3
X03663	X03663	164770	GEN-51	Colony stimulating factor 1 receptor	3732	5927T>C	3
X03663	X03663	164770	GEN-51	Colony stimulating factor 1 receptor	3951	3432T>C	3
X03747	X03747	182330	GEN-KR	ATPase, Na+/K+ transporting, beta 1 polypeptide	447	3651C>A	3
X03747	X03747	182330	GEN-KR	ATPase, Na+/K+ transporting, beta 1 polypeptide	1516	321G>A	S
X03747	X03747	182330	GEN-KR	ATPase, Na+/K+ transporting, beta 1 polypeptide	2182	1390G>T	3
CYBB	X04011	306400	GEN-13S	Human mRNA of X-CGD gene involved in chronic granulomatous disease located on chromosome X	2517	2056C>T	3
CYBB	X04011	306400	GEN-13S	Human mRNA of X-CGD gene involved in chronic granulomatous disease located on chromosome X	2544	2310A>G	3
CYBB	X04011	306400	GEN-13S	Human mRNA of X-CGD gene involved in chronic granulomatous disease located on chromosome X	2831	2337A>T	3
CAT	X04076	115500	GEN-13P	Human kidney mRNA for catalase	51	2624T>C	3
CAT	X04076	115500	GEN-13P	Human kidney mRNA for catalase	218	(-20)T>C	5
CAT	X04076	115500	GEN-13P	Human kidney mRNA for catalase	1237	148C>T	L50F
						1167T>C	S

CAT	X04076	115500	13P GEN-13P	catalase Human kidney mRNA for	1325	1255C>T	S
CAT	X04076	115500	GEN-13P	catalase Human kidney mRNA for	2131	2061A>C	3
HMBS	X04217	176000	GEN-145	catalase Human mRNA for	121	40G>T	A14S
				porphobilinogen deaminase (PBG-D, EC			
				4.3.1.8)			
X04409	X04409	139320	GEN-7Q	Guanine nucleotide binding protein (G protein), alpha	363	351C>T	S
				stimulating activity			
X04409	X04409	139320	GEN-7Q	polypeptide 1 Guanine nucleotide binding	525	513C>T	S
				protein (G protein), alpha			
				stimulating activity			
X04409	X04409	139320	GEN-7Q	polypeptide 1 Guanine nucleotide binding	967	955C>A	R319S
				protein (G protein), alpha			
				stimulating activity			
X04409	X04409	139320	GEN-7Q	polypeptide 1 Guanine nucleotide binding	1023	1011C>A	S
				protein (G protein), alpha			
				stimulating activity			
X04409	X04409	139320	GEN-7Q	polypeptide 1 Guanine nucleotide binding	1083	1071C>T	S
				protein (G protein), alpha			
				stimulating activity			
X04409	X04409	139320	GEN-7Q	polypeptide 1 Guanine nucleotide binding	1213	1201T>G	3
				protein (G protein), alpha			
				stimulating activity			
X04409	X04409	139320	GEN-7Q	polypeptide 1 Guanine nucleotide binding	1450	1438A>C	3
				protein (G protein), alpha			
				stimulating activity			
X04526	X04526	139380	GEN-7R	polypeptide 1 Guanine nucleotide binding	426	146G>C	R49T
				protein (G protein), beta			
THBS1	X04665	188060	GEN-151	polypeptide 1 Human mRNA for	145	70T>G	S24A

THBS1	X04665	188060	GEN-151	thrombospondin	Human mRNA for 903	828G>A	S
THBS1	X04665	188060	GEN-151	thrombospondin	Human mRNA for 1485	1410C>T	S
THBS1	X04665	188060	GEN-151	thrombospondin	Human mRNA for 3667	3592C>T	3
THBS1	X04665	188060	GEN-151	thrombospondin	Human mRNA for 3866	3791G>A	3
X05199	X05199	173350	GEN-PU	thrombospondin	Human mRNA for 384	330C>T	S
X05199	X05199	173350	GEN-PU	plasminogen	Human mRNA for 825	771C>T	S
X05199	X05199	173350	GEN-PU	plasminogen	Human mRNA for 996	942C>T	S
X05199	X05199	173350	GEN-PU	plasminogen	Human mRNA for 1137	1083A>G	S
X05199	X05199	173350	GEN-PU	plasminogen	Human mRNA for 1485	1431C>T	S
X05199	X05199	173350	GEN-PU	plasminogen	Human mRNA for 2340	2286T>G	S
X05199	X05199	173350	GEN-PU	plasminogen	Human mRNA for 2532	2478G>A	3
X05199	X05199	173350	GEN-PU	plasminogen	Human mRNA for 2606	2552T>G	3
X06318	X06318	176970	GEN-KY	plasminogen	Protein kinase C, beta 1 83	(-54)G>C	5
X06318	X06318	176970	GEN-KY	Protein kinase C, beta 1 940	804G>A		S
X06318	X06318	176970	GEN-KY	Protein kinase C, beta 1 1327	1191T>C		S
X06318	X06318	176970	GEN-KY	Protein kinase C, beta 1 1906	1770C>T		S
PDGFA	X06374	173430	GEN-19E	Human mRNA for platelet-derived growth factor	Human mRNA for platelet-derived growth factor PDGF-A	1820C>T	3
PDGFA	X06374	173430	GEN-19E	Human mRNA for platelet-derived growth factor	Human mRNA for platelet-derived growth factor PDGF-A	1864C>T	3
RAF1	X06409	164760	GEN-19K	Human mRNA fragment for activated c-raf-1 (exons 8-17)	Human mRNA fragment for activated c-raf-1 (exons 8-17)	487T>C	3
RAF1	X06409	164760	GEN-19K	Human mRNA fragment for activated c-raf-1 (exons 8-17)	Human mRNA fragment for activated c-raf-1 (exons 8-17)	1948C>T	3

RAF1	X06409	164760	GEN-19K	Human mRNA fragment for activated c-raf-1 (exons 8-17)	1993C>A	3
X06562	X06562	600946	GEN-6D	Growth hormone receptor	3349A>T	3
X06562	X06562	600946	GEN-6D	Growth hormone receptor	4102G>A	3
X07523	X07523	134371	GEN-1E5	Human mRNA for truncated form of complement factor H	1097G>A	G366E
X07523	X07523	134371	GEN-1E5	Human mRNA for truncated form of complement factor H	1204T>C	Y402H
SOD2	X07834	147460	GEN-1ES	Human mRNA for manganese superoxide dismutase (EC 1.15.1.1)	40C>G	P14A
SOD2	X07834	147460	GEN-1ES	Human mRNA for manganese superoxide dismutase (EC 1.15.1.1)	47T>C	V16A
SOD2	X07834	147460	GEN-1ES	Human mRNA for manganese superoxide dismutase (EC 1.15.1.1)	194C>A	T65N
SOD2	X07834	147460	GEN-1ES	Human mRNA for manganese superoxide dismutase (EC 1.15.1.1)	245T>C	I82T
TNNC1	X07897	191040	GEN-1EW	Human mRNA for slow skeletal troponin C (TnC)	208G>C	G70R
TNNC1	X07897	191040	GEN-1EW	Human mRNA for slow skeletal troponin C (TnC)	223G>T	D75Y
ITGB1	X07979	135630	GEN-4E5	Human mRNA for fibronectin receptor beta subunit	1086A>C	S
ITGB1	X07979	135630	GEN-4E5	Human mRNA for fibronectin receptor beta subunit	1176A>C	S
ITGB1	X07979	135630	GEN-4E5	Human mRNA for fibronectin receptor beta subunit	2610T>C	3
ITGB1	X07979	135630	GEN-4E5	Human mRNA for fibronectin receptor beta subunit	2775T>A	3
ITGB1	X07979	135630	GEN-4E5	Human mRNA for fibronectin receptor beta subunit	3236A>G	3

ITGB1	X07979	135630	4E5	fibronectin receptor beta subunit	3531	3428G>A	3
ANX5	X12454	131230	GEN-1M2	Human mRNA for vascular anticoagulant	128	(-1)C>T	5
ANX5	X12454	131230	GEN-1M2	Human mRNA for vascular anticoagulant	1413	1285T>G	3
ANX5	X12454	131230	GEN-1M2	Human mRNA for vascular anticoagulant	1431	1303C>T	3
ANX5	X12454	131230	GEN-1M2	Human mRNA for vascular anticoagulant	1518	1390G>A	3
X13561	X13561	147910	GEN-1OH	Human mRNA for 54 preprokallikrein (EC 3.4.21)	54	18G>T	S
X13561	X13561	147910	GEN-1OH	Human mRNA for 441 preprokallikrein (EC 3.4.21)	441	405T>C	S
X13561	X13561	147910	GEN-1OH	Human mRNA for 469 preprokallikrein (EC 3.4.21)	469	433G>C	E145Q
X13561	X13561	147910	GEN-1OH	Human mRNA for 592 preprokallikrein (EC 3.4.21)	592	556A>G	K186E
X13589	X13589	107910	GEN-56	Cytochrome P450, subfamily XIX (aromatization of androgens)	364	240A>G	S
X13589	X13589	107910	GEN-56	Cytochrome P450, subfamily XIX (aromatization of androgens)	914	790C>T	R264C
X13589	X13589	107910	GEN-56	Cytochrome P450, subfamily XIX (aromatization of androgens)	914	790C>T	R264C
X13589	X13589	107910	GEN-56	Cytochrome P450, subfamily XIX (aromatization of androgens)	1655	1531C>T	3
X13589	X13589	107910	GEN-56	Cytochrome P450, subfamily XIX (aromatization of androgens)	1796	1672G>T	3

X13629	X13629	107690	GEN-100	Human intestinal mRNA for apolipoprotein A-IV	881	836G>A	R279K
X13629	X13629	107690	GEN-100	Human intestinal mRNA for apolipoprotein A-IV	1185	1140G>T	Q380H
X13629	X13629	107690	GEN-100	Human intestinal mRNA for apolipoprotein A-IV	1302	1257*1258ins CTGT	F
X13916	X13916	107770	GEN-1Q1	Human mRNA for LDL-receptor related protein	1636	1170T>C	S
X13916	X13916	107770	GEN-1Q1	Human mRNA for LDL-receptor related protein	1675	1209C>T	S
X13916	X13916	107770	GEN-1Q1	Human mRNA for LDL-receptor related protein	2805	2339C>T	T780I
X13916	X13916	107770	GEN-1Q1	Human mRNA for LDL-receptor related protein	3853	3387T>C	S
X13916	X13916	107770	GEN-1Q1	Human mRNA for LDL-receptor related protein	6443	5977C>T	R1993W
X13916	X13916	107770	GEN-1Q1	Human mRNA for LDL-receptor related protein	7036	6570C>T	S
X13916	X13916	107770	GEN-1Q1	Human mRNA for LDL-receptor related protein	8608	8142G>A	S
X13916	X13916	107770	GEN-1Q1	Human mRNA for LDL-receptor related protein	8923	8457C>T	S
X13916	X13916	107770	GEN-1Q1	Human mRNA for LDL-receptor related protein	9034	8568G>T	S
X13916	X13916	107770	GEN-1Q1	Human mRNA for LDL-receptor related protein	9040	8574C>T	S
X13916	X13916	107770	GEN-1Q1	Human mRNA for LDL-receptor related protein	9391	8925T>C	S
CLU	X14723	185430	GEN-1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	131	84C>T	S
CLU	X14723	185430	GEN-1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	429	382G>T	V128F
CLU	X14723	185430	GEN-1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	836	789C>T	S
CLU	X14723	185430	GEN-1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	1234	1187C>T	S396L

CLU	X14723	185430	GEN- 1SB	for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	1372	1325A>T	Y442F
CLU	X14723	185430	GEN- 1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	1482	1435C>T	3
CLU	X14723	185430	GEN- 1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	1548	1501C>T	3
CLU	X14723	185430	GEN- 1SB	Human SP-40,40 mRNA for complement-associated protein SP-40,40 alpha-1 and beta-1 chain	1645	1598A>T	3
CHRNA1	X14830	100710	GEN- 4EK	Nicotinic, Cholinergic receptor beta 1	1375	1359C>T	S
CHRNA1	X14830	100710	GEN- 4EK	Nicotinic, Cholinergic receptor beta 1	1591	1575T>C	3
X15263	X15263	None	GEN- 4EQ	Muscarinic receptor, 1144 CHRM1	1144	1044G>A	S
X15357	X15357	108960	GEN- KUV	Human mRNA for natriuretic peptide receptor (ANP-A receptor)	1066	1023G>C	M341I
X15357	X15357	108960	GEN- KUV	Human mRNA for natriuretic peptide receptor (ANP-A receptor)	1657	1614C>T	S
X15357	X15357	108960	GEN- KUV	Human mRNA for natriuretic peptide receptor (ANP-A receptor)	2859	2816G>A	R939Q
X15357	X15357	108960	GEN- KUV	Human mRNA for natriuretic peptide receptor (ANP-A receptor)	2983	2940G>A	S
X15357	X15357	108960	GEN- KUV	Human mRNA for natriuretic peptide receptor (ANP-A receptor)	3259	3216delC	F
X15357	X15357	108960	GEN- KUV	Human mRNA for natriuretic peptide receptor (ANP-A receptor)	3589	3546^3547ins	F

		KUV	natriuretic peptide receptor (ANP-A receptor)		GAAA	
PACE	X17094	GEN-12V	Human fur mRNA for furin 399	183C>T	S	
PACE	X17094	GEN-12V	Human fur mRNA for furin 1692	1476C>T	S	
PACE	X17094	GEN-12V	Human fur mRNA for furin 2067	1851C>G	S	
PACE	X17094	GEN-12V	Human fur mRNA for furin 2725	2509T>C	3	
PACE	X17094	GEN-12V	Human fur mRNA for furin 2855	2639C>A	3	
PACE	X17094	GEN-12V	Human fur mRNA for furin 2988	2772G>A	3	
PACE	X17094	GEN-12V	Human fur mRNA for furin 3234	3018C>T	3	
PACE	X17094	GEN-12V	Human fur mRNA for furin 3625	3409A>G	3	
PACE	X17094	GEN-12V	Human fur mRNA for furin 3883	3667C>T	3	
PACE	X17094	GEN-12V	Human fur mRNA for furin 4053	3837A>G	3	
X51362	X51362	GEN-31W	Dopamine Receptor D2 588	423G>A	S	
X51362	X51362	GEN-31W	Dopamine Receptor D2 1104	939C>T	S	
X51362	X51362	GEN-31W	Dopamine Receptor D2 1122	957T>C	S	
X51362	X51362	GEN-31W	Dopamine Receptor D2 1248	1083A>G	S	
X51362	X51362	GEN-31W	Dopamine Receptor D2 1488	1323T>C	S	
X51362	X51362	GEN-31W	Dopamine Receptor D2 1548	1383A>G	3	
X51362	X51362	GEN-31W	Dopamine Receptor D2 2361	2196C>T	3	
X51416	X51416	GEN-57	STEROID HORMONE 2285 RECEPTOR ERR1	2222G>A	3	
FLT1	X51602	GEN-329	Human flt mRNA for 192 receptor-related tyrosine kinase	(-58)C>T	5	

FLT1	X51602	165070	GEN-329	Human flt mRNA for receptor-related tyrosine kinase	1723	1474C>T	S
FLT1	X51602	165070	GEN-329	Human flt mRNA for receptor-related tyrosine kinase	1953	1704G>A	S
FLT1	X51602	165070	GEN-329	Human flt mRNA for receptor-related tyrosine kinase	3061	2812A>G	M938V
FLT1	X51602	165070	GEN-329	Human flt mRNA for receptor-related tyrosine kinase	3150	2901G>A	S
FLT1	X51602	165070	GEN-329	Human flt mRNA for receptor-related tyrosine kinase	4497	4248T>G	3
FLT1	X51602	165070	GEN-329	Human flt mRNA for receptor-related tyrosine kinase	5295	5046*5047ins GAG	3
FLT1	X51602	165070	GEN-329	Human flt mRNA for receptor-related tyrosine kinase	6976	6727G>A	3
FLT1	X51602	165070	GEN-329	Human flt mRNA for receptor-related tyrosine kinase	7013	6764T>G	3
FGFR1	X51803	136350	GEN-32G	Human mRNA for fibroblast growth factor (FGF) receptor	276	159T>G	S
EDN3	X52001	131242	GEN-33E	Endothelin 3	1262	1152G>A	3
EDN3	X52001	131242	GEN-33E	Endothelin 3	1649	1539C>G	3
EDN3	X52001	131242	GEN-33E	Endothelin 3	1700	1590C>T	3
EDN3	X52001	131242	GEN-33E	Endothelin 3	1742	1632C>T	3
EDN3	X52001	131242	GEN-33E	Endothelin 3	1797	1687C>T	3
EDN3	X52001	131242	GEN-33E	Endothelin 3	1914	1804G>C	3
EDN3	X52001	131242	GEN-33E	Endothelin 3	2040	1930C>T	3

X52425	X52425	147781	GEN-59	Interleukin 4 receptor	3044	2869G>A	3
X52425	X52425	147781	GEN-59	Interleukin 4 receptor	3289	3114A>G	3
X52425	X52425	147781	GEN-59	Interleukin 4 receptor	3391	3216C>T	3
X52479	X52479	176960	GEN-LM	Protein kinase C, alpha	908	881A>C	D294A
FGFR2	X52832	176943	GEN-341	Human bek mRNA for fibroblast growth factor receptor-BEK	338	159A>G	S
FGFR2	X52832	176943	GEN-341	Human bek mRNA for fibroblast growth factor receptor-BEK	2903	2724A>T	3
CHRNA3	X53559	118503	GEN-341	Nicotinic, Cholinergic receptor alpha 3	212	212A>G	D71G
CHRNA3	X53559	118503	GEN-341	Nicotinic, Cholinergic receptor alpha 3	552	552C>T	S
TNNI3	X54163	191044	GEN-34U	Human mRNA for cardiac troponin I	626	537G>A	S
FGFR4	X57205	134935	GEN-37M	Human FGFR-4 mRNA for fibroblast growth factor receptor (FGFR-4)	83	28G>A	V10I
FGFR4	X57205	134935	GEN-37M	Human FGFR-4 mRNA for fibroblast growth factor receptor (FGFR-4)	217	162T>G	S
YWHAB	X57346	601289	GEN-37R	H.sapiens mRNA for HS1 protein	432	60C>A	S
YWHAB	X57346	601289	GEN-37R	H.sapiens mRNA for HS1 protein	1135	763T>C	3
X57830	X57830	182135	GEN-7V	Serotonin 5-HT2 receptor	247	102T>C	S
GPX3	X58295	138321	GEN-38S	Human GPx-3 mRNA for plasma glutathione peroxidase	821	773C>T	3
GPX3	X58295	138321	GEN-38S	Human GPx-3 mRNA for plasma glutathione peroxidase	979	931G>A	3
GPX3	X58295	138321	GEN-38S	Human GPx-3 mRNA for plasma glutathione peroxidase	1187	1139T>G	3
GPX3	X58295	138321	GEN-38S	Human GPx-3 mRNA for plasma glutathione peroxidase	1354	1306C>T	3
GPX3	X58295	138321	GEN-38S	Human GPx-3 mRNA for plasma glutathione peroxidase	1443	1395C>T	3

GPX3	X58295	138321	38S	plasma glutathione peroxidase	1468C>A	3
			GEN-38S	Human GPx-3 mRNA for 1516		
GPX3	X58295	138321	38S	plasma glutathione peroxidase	1533C>T	3
			GEN-38S	Human GPx-3 mRNA for 1581		
X58377	X58377	147681	38V	plasma glutathione peroxidase	744A>G	3
			GEN-38V	Interleukin 11 807		
X58377	X58377	147681	38V	Interleukin 11 927	864T>G	3
			GEN-38V	Interleukin 11 1964	1901T>C	3
DRD1	X58987	126449	4EH	D1 dopaminergic receptor 229	(-48)A>G	5
			GEN-4EH	D1 dopaminergic receptor 366	90G>A	S
DRD1	X58987	126449	4EH	D1 dopaminergic receptor 474	198G>A	S
			GEN-4EH	D1 dopaminergic receptor 1539	1263G>A	S
DRD1	X58987	126449	4EH	D1 dopaminergic receptor 2040	1764A>C	3
			GEN-4EH	D1 dopaminergic receptor 2045	1769C>A	3
X59842	X59842	600214	3A3	Human PBX2 mRNA 2339	2043T>G	3
X60069	X60069	231950	3AJ	Human mRNA for 102	(-257)G>A	5
			GEN-3AJ	pancreatic gamma-glutamyltransferase	(-23)C>T	5
X60069	X60069	231950	3AJ	Human mRNA for 336		
			GEN-3AJ	pancreatic gamma-glutamyltransferase	815C>T	A272V
X60069	X60069	231950	3AJ	Human mRNA for 1173		
			GEN-3AJ	pancreatic gamma-glutamyltransferase	815C>T	A272V
X60069	X60069	231950	3AJ	Human mRNA for 1399	1041C>T	S
			GEN-3AJ	pancreatic gamma-glutamyltransferase		

X60069	X60069	231950	GEN-3AJ	pancreatic gamma-glutamyltransferase Human mRNA for 1409	1051G>T	A351S
X60069	X60069	231950	GEN-3AJ	pancreatic gamma-glutamyltransferase Human mRNA for 1482	1124C>T	T375M
X60069	X60069	231950	GEN-3AJ	pancreatic gamma-glutamyltransferase Human mRNA for 1591	1233G>A	S
X60069	X60069	231950	GEN-3AJ	pancreatic gamma-glutamyltransferase Human mRNA for 1624	1266C>T	S
X60069	X60069	231950	GEN-3AJ	pancreatic gamma-glutamyltransferase Human mRNA for 1637	1279C>A	P427T
X60069	X60069	231950	GEN-3AJ	pancreatic gamma-glutamyltransferase Human mRNA for 1651	1293C>T	S
X60069	X60069	231950	GEN-3AJ	pancreatic gamma-glutamyltransferase Human mRNA for 1662	1304T>C	V435A
X60069	X60069	231950	GEN-3AJ	pancreatic gamma-glutamyltransferase Human mRNA for 1783	1425A>G	S
X60069	X60069	231950	GEN-3AJ	pancreatic gamma-glutamyltransferase Human mRNA for 1794	1436C>T	T479M
X60069	X60069	231950	GEN-3AJ	pancreatic gamma-glutamyltransferase Human mRNA for 1795	1437G>A	S
X60069	X60069	231950	GEN-3AJ	pancreatic gamma-glutamyltransferase Human mRNA for 1981	1623C>T	S
X60069	X60069	231950	GEN-3AJ	pancreatic gamma-glutamyltransferase Human mRNA for 2007	1649C>T	T550M
X60069	X60069	231950	GEN-3AJ	pancreatic gamma-glutamyltransferase Human mRNA for 2031	1673C>T	S558L

X60069	X60069	231950	GEN-3AJ	Human mRNA for pancreatic gamma-glutamyltransferase	2047	1689C>T	S
X60069	X60069	231950	GEN-3AJ	Human mRNA for pancreatic gamma-glutamyltransferase	2147	1789C>T	3
X60069	X60069	231950	GEN-3AJ	Human mRNA for pancreatic gamma-glutamyltransferase	2176	1818C>T	3
X60069	X60069	231950	GEN-3AJ	Human mRNA for pancreatic gamma-glutamyltransferase	2224	1866C>A	3
X60957	X60957	600222	GEN-3BF	Human mRNA for putative receptor tyrosine kinase	2194	2158G>A	A720T
X61157	X61157	109635	GEN-23	Adrenergic receptor (Beta kinase 1-phosphorylates beta adrenergic receptor)	203	96A>C	S
X61157	X61157	109635	GEN-23	Adrenergic receptor (Beta kinase 1-phosphorylates beta adrenergic receptor)	1372	1265A>G	H422R
X61157	X61157	109635	GEN-23	Adrenergic receptor (Beta kinase 1-phosphorylates beta adrenergic receptor)	1501	1394G>A	R465K
X61157	X61157	109635	GEN-23	Adrenergic receptor (Beta kinase 1-phosphorylates beta adrenergic receptor)	1766	1659C>T	S
X61157	X61157	109635	GEN-23	Adrenergic receptor (Beta kinase 1-phosphorylates beta adrenergic receptor)	1823	1716T>C	S
X61157	X61157	109635	GEN-23	Adrenergic receptor (Beta kinase 1-phosphorylates beta adrenergic receptor)	2976	2869G>A	3
NFKB2	X61498	164012	GEN-3BW	Adrenergic receptor (Beta kinase 1-phosphorylates beta adrenergic receptor)	2457	2294C>T	P765L
KDR	X61656	191306	GEN-3BZ	H.sapiens mRNA for NF-kB subunit	2308	2308A>G	T770A
KDR	X61656	191306	GEN-3BZ	H.sapiens mRNA for growth factor receptor tyrosine kinase	2353	2353G>C	G785R

KDR	X61656	191306	GEN-3BZ	H.sapiens mRNA for growth factor receptor tyrosine kinase	2499C>G	N833K
KDR	X61656	191306	GEN-3BZ	H.sapiens mRNA for growth factor receptor tyrosine kinase	2537A>T	E846V
KDR	X61656	191306	GEN-3BZ	H.sapiens mRNA for growth factor receptor tyrosine kinase	4123G>C	3
X63359	X63359	600070	GEN-3DC	H.sapiens UGT2B10 mRNA for udp glucuronosyltransferase	1506C>T	S
X63359	X63359	600070	GEN-3DC	H.sapiens UGT2B10 mRNA for udp glucuronosyltransferase	2704G>A	3
ACLY	X64330	108728	GEN-3F0	H.sapiens mRNA for ATP-citrate lyase	3914G>T	3
ACLY	X64330	108728	GEN-3F0	H.sapiens mRNA for ATP-citrate lyase	4145A>C	3
X65019	X65019	147678	GEN-6G	INTERLEUKIN 1 BETA 51 CONVERTASE PRECURSOR	44G>A	R15H
X65019	X65019	147678	GEN-6G	INTERLEUKIN 1 BETA 116 CONVERTASE PRECURSOR	109A>C	K37Q
X65019	X65019	147678	GEN-6G	INTERLEUKIN 1 BETA 261 CONVERTASE PRECURSOR	254G>A	G85E
X66364	X66364	123831	GEN-3GM	H.sapiens mRNA for PSSALRE for serine/threonine protein kinase	471T>G	C157W
X66403	X66403	100725	GEN-5D	Nicotinic, Cholinergic receptor epsilon polypeptide	2225G>T	3
X66403	X66403	100725	GEN-5D	Nicotinic, Cholinergic receptor epsilon polypeptide	2322A>G	3
X66403	X66403	100725	GEN-5D	Nicotinic, Cholinergic receptor epsilon polypeptide	2353G>T	3

X69117	X69117	109636	GEN-5G	BETA-ADRENERGIC RECEPTOR KINASE 2	1182	1182T>C	S
X69117	X69117	109636	GEN-5G	BETA-ADRENERGIC RECEPTOR KINASE 2	1609	1609G>A	E537K
X69141	X69141	184420	GEN-3J9	H.sapiens mRNA for squalene synthase	112	21T>C	S
X69141	X69141	184420	GEN-3J9	H.sapiens mRNA for squalene synthase	292	201C>T	S
X69141	X69141	184420	GEN-3J9	H.sapiens mRNA for squalene synthase	1436	1345T>C	3
X69141	X69141	184420	GEN-3J9	H.sapiens mRNA for squalene synthase	1579	1488T>C	3
X69141	X69141	184420	GEN-3J9	H.sapiens mRNA for squalene synthase	1621	1530C>T	3
X69141	X69141	184420	GEN-3J9	H.sapiens mRNA for squalene synthase	1719	1628A>C	3
X69141	X69141	184420	GEN-3J9	H.sapiens mRNA for squalene synthase	1904	1813G>C	3
X70811	X70811	109691	GEN- 3KK	beta-3-adrenergic receptor	315	190T>C	W64R
X70811	X70811	109691	GEN- 3KK	beta-3-adrenergic receptor	315	190T>C	W64R
X71440	X71440	None	GEN- 3KS	H.sapiens mRNA for peroxisomal acyl-CoA oxidase	949	936G>C	M312I
GPX4	X71973	138322	GEN-3L1	H.sapiens GPx-4 mRNA for phospholipid hydroperoxide glutathione peroxidase	718	638T>C	3
GPX4	X71973	138322	GEN-3L1	H.sapiens GPx-4 mRNA for phospholipid hydroperoxide glutathione peroxidase	837	757C>A	3
GPX4	X71973	138322	GEN-3L1	H.sapiens GPx-4 mRNA for phospholipid hydroperoxide glutathione peroxidase	882	802A>C	3
NOS2A	X73029	163730	GEN- 3LW	H.sapiens mRNA for nitric oxide synthase	1380	1155C>T	S
NOS2A	X73029	163730	GEN- 3LW	H.sapiens mRNA for nitric oxide synthase	1503	1278C>T	S

NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	2048	1823C>T	S608L
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	2287	2062G>A	G688S
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	2339	2114A>G	D705G
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	2583	2358T>C	S
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	2982	2757A>G	S
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	3022	2797C>G	R933G
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	3051	2826C>T	S
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	3693	3468T>C	3
NOS2A	X73029	163730	GEN-3LW	H.sapiens mRNA for nitric oxide synthase	3715	3490G>A	3
PREP	X74496	600400	GEN-3N8	Prolyl Endopeptidase	390	390T>C	S
PREP	X74496	600400	GEN-3N8	Prolyl Endopeptidase	1051	1051T>G	L351V
PREP	X74496	600400	GEN-3N8	Prolyl Endopeptidase	1125	1125C>T	S
PREP	X74496	600400	GEN-3N8	Prolyl Endopeptidase	1363	1363G>A	V455M
X75299	X75299	192321	GEN-3NU	H.sapiens HIVR mRNA for vasoactive intestinal peptide (VIP) receptor	1915	1904T>C	3
X75299	X75299	192321	GEN-3NU	H.sapiens HIVR mRNA for vasoactive intestinal peptide (VIP) receptor	2475	2464T>C	3
MTP	X75500	157147	GEN-3O7	H.sapiens mRNA for microsomal triglyceride transfer protein	1847	1823T>G	F608C
MTP	X75500	157147	GEN-3O7	H.sapiens mRNA for microsomal triglyceride transfer protein	3231	3207G>A	3
X75913	X75913	601269	GEN-3OG	H.sapiens mRNA for gC1q-R	1052	974A>G	3
X75913	X75913	601269	GEN-3OG	H.sapiens mRNA for gC1q-R	1074	996T>C	3

		3OG	R		
X76180	X76180	600228	GEN-N5	Solute carrier family 9 (sodium/hydrogen exchanger), isoform 1 (antiporter, Na ⁺ /H ⁺ , amiloride sensitive)	1802G>A G601D
	LIPA	X76488	278000	H.sapiens mRNA for lysosomal acid lipase	46A>C T16P
	LIPA	X76488	278000	H.sapiens mRNA for lysosomal acid lipase	67G>A G23R
	LIPA	X76488	278000	H.sapiens mRNA for lysosomal acid lipase	822G>A M274I
	LIPA	X76488	278000	H.sapiens mRNA for lysosomal acid lipase	1386C>T 3
	LIPA	X76488	278000	H.sapiens mRNA for lysosomal acid lipase	2109A>T 3
	LIPA	X76488	278000	H.sapiens mRNA for lysosomal acid lipase	2294C>T 3
X77094	X77094	601488	GEN-3P2	H.sapiens mRNA for p40phox	735C>T S
YWHAH	X78138	113508	GEN-3QU	H.sapiens 14-3-3 eta subtype mRNA	753A>G 3
YWHAH	X78138	113508	GEN-3QU	H.sapiens 14-3-3 eta subtype mRNA	760G>A 3
YWHAH	X78138	113508	GEN-3QU	H.sapiens 14-3-3 eta subtype mRNA	1187C>T 3
X78282	X78282	601292	GEN-LVF	H.sapiens mRNA for aryl sulfotransferase (ST1A2)	895T>C 3
X78706	X78706	600184	GEN-2A	Carnitine Acetyltransferase	1922G>A 3
X78706	X78706	600184	GEN-2A	Carnitine Acetyltransferase	2378G>A 3
X78706	X78706	600184	GEN-2A	Carnitine Acetyltransferase	2382G>A 3
X79483	X79483	602399	GEN-LPR	H.sapiens ERK6 mRNA for extracellular signal regulated kinase	1254T>G 3
TNNT2	X79857	191045	GEN-3TJ	H.sapiens HTNT4 mRNA for cardiac troponin T	80G>T W27L
TNNT2	X79857	191045	GEN-3TJ	H.sapiens HTNT4 mRNA for cardiac troponin T	114G>C S
TNNT2	X79857	191045	GEN-3TJ	H.sapiens HTNT4 mRNA for cardiac troponin T	193G>T F

TNNT2	X79857	191045	GEN-3TJ	H.sapiens HTNT4 mRNA 920 for cardiac troponin T	809C>A	3
X80230	X80230	603251	GEN-3UM	H.sapiens mRNA (clone C- 25 2k) mRNA for serine/threonine protein kinase	(-74)C>T	5
X80230	X80230	603251	GEN-3UM	H.sapiens mRNA (clone C- 77 2k) mRNA for serine/threonine protein kinase	(-22)C>T	5
X80230	X80230	603251	GEN-3UM	H.sapiens mRNA (clone C- 1516 2k) mRNA for serine/threonine protein kinase	1418G>A	3
X80230	X80230	603251	GEN-3UM	H.sapiens mRNA (clone C- 1574 2k) mRNA for serine/threonine protein kinase	1476A>G	3
X81411	X81411	None	GEN-4EY	Serotonin 5-HT receptors 75 5-HT5a	76A>T	3
X83582	X83582	600734	GEN-3YD	Potassium channel Kir3.4 171	171C>T	S
X83582	X83582	600734	GEN-3YD	Potassium channel Kir3.4 834	834C>T	S
X83861	X83861	176806	GEN-5H	Prostaglandin E receptor 3 387 (subtype EP3) {alternative products}	180C>G	S
X84213	X84213	600516	GEN-3ZC	H.sapiens BAK mRNA for 32 BCI-2 homologue	(-161)C>T	5
X84213	X84213	600516	GEN-3ZC	H.sapiens BAK mRNA for 317 BCI-2 homologue	125G>A	R42H
X84213	X84213	600516	GEN-3ZC	H.sapiens BAK mRNA for 435 BCI-2 homologue	243C>T	S
X84213	X84213	600516	GEN-3ZC	H.sapiens BAK mRNA for 616 BCI-2 homologue	424G>A	V142I
X84213	X84213	600516	GEN-3ZC	H.sapiens BAK mRNA for 663 BCI-2 homologue	471C>T	S
X84213	X84213	600516	GEN-3ZC	H.sapiens BAK mRNA for 900 BCI-2 homologue	708T>C	3
X84213	X84213	600516	GEN-3ZC	H.sapiens BAK mRNA for 974 BCI-2 homologue	782C>T	3

X86097	X86097	600967	GEN-400	H.sapiens mRNA for E2F-5 protein	162	132G>C	S
X86097	X86097	600967	GEN-400	H.sapiens mRNA for E2F-5 protein	1281	1251T>C	3
X86097	X86097	600967	GEN-400	H.sapiens mRNA for E2F-5 protein	1725	1695A>C	3
X86681	X86681	602110	GEN-41E	H.sapiens mRNA for nucleolar protein, HNP36	1725	1340G>A	3
X93086	X93086	109750	GEN-48G	H.sapiens mRNA for biliverdin IX alpha reductase	669	609G>A	S
X93086	X93086	109750	GEN-48G	H.sapiens mRNA for biliverdin IX alpha reductase	720	660A>G	S
X95190	X95190	601641	GEN-49Y	H.sapiens mRNA for Branched chain Acyl-CoA Oxidase	1394	1302C>T	S
X95190	X95190	601641	GEN-49Y	H.sapiens mRNA for Branched chain Acyl-CoA Oxidase	1934	1842C>A	S
X97058	X97058	602451	GEN-48B	P2 purinoceptor (P2Y6)	121	(-156)T>G	5
R9R2	X98330	180902	GEN-4CB	H.sapiens mRNA for ryanodine receptor 2	13745	13624G>A	A4542T
R9R2	X98330	180902	GEN-4CB	H.sapiens mRNA for ryanodine receptor 2	15541	15420T>G	3
Y00285	Y00285	147280	GEN-6I	IGF-2 receptor	4613	4466G>A	S1489N
Y00285	Y00285	147280	GEN-6I	IGF-2 receptor	6371	6224C>T	T2075M
Y00285	Y00285	147280	GEN-6I	IGF-2 receptor	6813	6666C>T	S
Y00285	Y00285	147280	GEN-6I	IGF-2 receptor	7150	7003G>A	V2335M
Y00285	Y00285	147280	GEN-6I	IGF-2 receptor	8685	8538C>A	3
GPX1	Y00433	138320	GEN-TJ	Human mRNA for glutathione peroxidase (EC 1.11.1.9.)	504	186G>A	S
GPX1	Y00433	138320	GEN-TJ	Human mRNA for glutathione peroxidase (EC 1.11.1.9.)	610	292C>G	R98G
GPX1	Y00433	138320	GEN-TJ	Human mRNA for glutathione peroxidase (EC 1.11.1.9.)	911	593C>T	P198L

GPX1	Y00433	138320	GEN-TJ	Human mRNA for 1048 glutathione peroxidase (EC 1.11.1.9.)	730A>C	3
GPX1	Y00433	138320	GEN-TJ	Human mRNA for 1110 glutathione peroxidase (EC 1.11.1.9.)	792A>C	3
ALAS1	Y00451	125290	GEN-TE	Human mRNA for 5- aminolevulinate synthase	426T>G	S
ALAS1	Y00451	125290	GEN-TE	Human mRNA for 5- aminolevulinate synthase	525C>T	S
PAI2	Y00630	173390	GEN-U6	Human mRNA for Arg- Serpine (plasminogen activator-inhibitor 2, PAI-2)	358A>G	N120D
PAI2	Y00630	173390	GEN-U6	Human mRNA for Arg- Serpine (plasminogen activator-inhibitor 2, PAI-2)	1179T>G	S
PAI2	Y00630	173390	GEN-U6	Human mRNA for Arg- Serpine (plasminogen activator-inhibitor 2, PAI-2)	1690G>A	3
Y00692	Y00692	176880	GEN-6K	Anticoagulant protein S 785	586C>T	3
Y00692	Y00692	176880	GEN-6K	Anticoagulant protein S 910	711T>C	3
Y00692	Y00692	176880	GEN-6K	Anticoagulant protein S 1156	957G>T	3
Y00749	Y00749	131240	GEN-P7	Endothelin 1 846	594G>T	K198N
CR1	Y00816	120620	GEN-UG	Human mRNA for 207 complement receptor type 1 (CR1, C3b/C4b receptor, CD35)	180G>C	E60D
Y07683	Y07683	600843	GEN- 4F1	H. sapiens mRNA for P2X3 717 purinoceptor	552C>T	S
Y07683	Y07683	600843	GEN- 4F1	H. sapiens mRNA for P2X3 753 purinoceptor	588A>G	S
Y08110	Y08110	602005	GEN- 1FK	H. sapiens mRNA for 3641 mosaic protein LR11	3561T>G	S
Y08110	Y08110	602005	GEN- 1FK	H. sapiens mRNA for 3818 mosaic protein LR11	3738C>T	S
Y08110	Y08110	602005	GEN- 1FK	H. sapiens mRNA for 5158 mosaic protein LR11	5078G>A	S1693N
Y08110	Y08110	602005	GEN- 1FK	H. sapiens mRNA for 6571 mosaic protein LR11	6491G>A	R2164K
Y08756	Y08756	602164	GEN- 4EC	Serotonin 5-HT receptors 765 5-HT4	747T>C	S

Y09561	Y09561	None	GEN-4F4	H.sapiens mRNA for P2X7 receptor	835	809A>G	H270R
Y09561	Y09561	None	GEN-4F4	H.sapiens mRNA for P2X7 receptor	946	920G>A	R307Q
Y09561	Y09561	None	GEN-4F4	H.sapiens mRNA for P2X7 receptor	1068	1042G>A	A348T
Y09561	Y09561	None	GEN-4F4	H.sapiens mRNA for P2X7 receptor	1096	1070C>G	T357S
Y09561	Y09561	None	GEN-4F4	H.sapiens mRNA for P2X7 receptor	1405	1379A>G	Q460R
Y09561	Y09561	None	GEN-4F4	H.sapiens mRNA for P2X7 receptor	1589	1563C>G	H521Q
Y09561	Y09561	None	GEN-4F4	H.sapiens mRNA for P2X7 receptor	1590	1564G>A	V522I
Y09561	Y09561	None	GEN-4F4	H.sapiens mRNA for P2X7 receptor	1628	1602G>T	S
Y09561	Y09561	None	GEN-4F4	H.sapiens mRNA for P2X7 receptor	1759	1733G>A	R578Q
Y09561	Y09561	None	GEN-4F4	H.sapiens mRNA for P2X7 receptor	1772	1746G>A	S
Y10659	Y10659	300119	GEN-1J6	H.sapiens IL-13Ra mRNA	1116	1073G>A	G358D
IREB1	Z11559	147581	GEN-1KO	H.sapiens mRNA for iron regulatory factor	2855	2748T>C	3
IREB1	Z11559	147581	GEN-1KO	H.sapiens mRNA for iron regulatory factor	3162	3055C>A	3
IREB1	Z11559	147581	GEN-1KO	H.sapiens mRNA for iron regulatory factor	3460	3353A>T	3
Z11695	Z11695	176948	GEN-1L1	H.sapiens 40 kDa protein kinase related to rat ERK2	1287	1153G>A	3
Z11696	Z11696	601795	GEN-1L0	H.sapiens 44kDa protein kinase related to rat ERK1	449	449T>G	I150S
Z15108	Z15108	176982	GEN-1TE	H.sapiens mRNA for protein kinase C zeta	246	240T>C	S
Z15108	Z15108	176982	GEN-1TE	H.sapiens mRNA for protein kinase C zeta	1694	1688A>C	D563A
Z15108	Z15108	176982	GEN-1TE	H.sapiens mRNA for protein kinase C zeta	2033	2027G>A	3
Z15108	Z15108	176982	GEN-1TE	H.sapiens mRNA for protein kinase C zeta	2086	2080T>G	3
Z19585	Z19585	600715	GEN-22A	H.sapiens mRNA for thrombospondin-4	2135	2108G>A	C703Y

Z22555	Z22555	601040	GEN-264	H.sapiens encoding CLA-1 mRNA	1119	1050C>T	S
Z22555	Z22555	601040	GEN-264	H.sapiens encoding CLA-1 mRNA	2553	2484A>G	3
TPM1	Z24727	191010	GEN-280	H.sapiens tropomyosin isoform mRNA, complete CDS	585	259G>T	F
TPM1	Z24727	191010	GEN-280	H.sapiens tropomyosin isoform mRNA, complete CDS	606	280G>T	F
TPM1	Z24727	191010	GEN-280	H.sapiens tropomyosin isoform mRNA, complete CDS	668	342C>A	S
TPM1	Z24727	191010	GEN-280	H.sapiens tropomyosin isoform mRNA, complete CDS	780	454C>A	Q152K
TPM1	Z24727	191010	GEN-280	H.sapiens tropomyosin isoform mRNA, complete CDS	1333	1007T>C	3
TPM1	Z24727	191010	GEN-280	H.sapiens tropomyosin isoform mRNA, complete CDS	1356	1030A>G	3
TPM1	Z24727	191010	GEN-280	H.sapiens tropomyosin isoform mRNA, complete CDS	1553	1227T>G	3
Z26649	Z26649	600230	GEN-2B5	Phospholipase C beta-3	437	438C>T	3
Z26649	Z26649	600230	GEN-2B5	Phospholipase C beta-3	466	467G>A	3
Z26649	Z26649	600230	GEN-2B5	Phospholipase C beta-3	2664	2665C>T	3
Z26649	Z26649	600230	GEN-2B5	Phospholipase C beta-3	3168	3169G>T	3
CPO	Z28409	121300	GEN-2D8	H.sapiens coprox gene for coproporphyrinogen oxidase	1994	1994G>A	3
ECE1	Z35307	600423	GEN-2MA	Endothelin Converting Enzyme 1	1141	1104C>T	S
ECE1	Z35307	600423	GEN-2MA	Endothelin Converting Enzyme 1	1627	1590T>C	S
ECE1	Z35307	600423	GEN-2MA	Endothelin Converting Enzyme 1	1696	1659G>A	S

ECE1	Z35307	600423	2MA	Enzyme 1	1909G>A	V637M
	GEN-		GEN-	Endothelin Converting		
	2MA		2MA	Enzyme 1		
ECE1	Z35307	600423	GEN-	Endothelin Converting	2396G>A	3
	2MA		2MA	Enzyme 1		
Z35491	Z35491	601497	GEN-	H.sapiens mRNA for novel	37G>A	E13K
	2ME		2ME	glucocorticoid receptor-associated protein		
Z35491	Z35491	601497	GEN-	H.sapiens mRNA for novel	55G>A	E19K
	2ME		2ME	glucocorticoid receptor-associated protein		
Z35491	Z35491	601497	GEN-	H.sapiens mRNA for novel	1019A>C	3
	2ME		2ME	glucocorticoid receptor-associated protein		
Z48810	Z48810	602664	GEN-	H.sapiens mRNA for TX	1239A>C	3
	2YJ		2YJ	protease precursor		
Z69881	Z69881	601929	GEN-	H.sapiens mRNA for	2017G>A	A673T
	3JV		3JV	adenosine triphosphatase, calcium		
Z69881	Z69881	601929	GEN-	H.sapiens mRNA for	3630C>G	3
	3JV		3JV	adenosine triphosphatase, calcium		

Table 18. Identified
Variances in Genes or
Related Pathways
involved in Cancer and
Related Disorders

human DNA mismatch repair protein hMLH1/MutL	U07418	120436	SER252TER
human DNA mismatch repair protein hMLH1/MutL	U07418	120436	SER44PHE
human DNA mismatch repair protein hMLH1/MutL	U07418	120436	3-BP DEL LYS618DEL
human DNA mismatch repair protein hMLH1/MutL	U07418	120436	3.5-KB DEL
human DNA mismatch repair protein hMLH1/MutL	U07418	120436	G-to-A intron 5 splice junction
human DNA mismatch repair protein hMLH1/MutL	U07418	120436	370-BP DEL frameshift
human DNA mismatch repair protein hMLH1/MutL	U07418	120436	IVS14DS, 7-BP DEL AND 4-BP INS
human DNA mismatch repair protein hMLH1/MutL	U07418	120436	HIS329PRO
human DNA mismatch	U07418	120436	1784delT truncated

repair protein hMLH1/MutL human DNA mismatch	U07418	120436	676C-T ARG226TER
repair protein hMLH1/MutL human DNA mismatch	U07418	120436	GGG to TGG GLY67TRP
repair protein hMLH1/MutL human DNA mismatch	U07418	120436	A-->T codon 26
repair protein hMLH1/MutL human DNA mismatch	U07418	120436	GG-->AT 177 and 178
repair protein hMLH1/MutL human DNA mismatch	U07418	120436	-93 nt
repair protein hMLH1/MutL human DNA mismatch	U07418	120436	Val384Asp
repair protein hMLH1/MutL human DNA mismatch	U07418	120436	T insertion 3 splice site post exon 9
repair protein hMLH1/MutL human DNA mismatch	U07418	120436	deletion of codon 618K
repair protein hMLH1/MutL human DNA mismatch	U07418	120436	A-to-G transition exon 6
repair protein hMLH1/MutL human DNA mismatch	U07418	120436	exon 5 missense

hMLH1/MutL	U07418	120436	exon 9 missense
human DNA mismatch repair protein			
hMLH1/MutL	U54831	126431	reported
topoisomerase IIb	M60761	156569	GGA to AGA GLY160ARG
O6 alkylguanine-DNA alkyltransferase	M26761	100640	none found
class I aldehyde dehydrogenase	AF020918	*****	none found
glutathione-S-transferase GSTA4	J05459	138390	3bp deletion intron 6
glutathione-S-transferase GSTM3	X79389	600436	null genotype
glutathione-S-transferase GSTT1	L38503	600437	none found
glutathione-S-transferase GSTT2	Y00433	138320	P197L
glutathione peroxidase GPx1	Y00433	138320	1167T/C Silent
glutathione peroxidase GPx1	X68314	138319	A/T intron
glutathione peroxidase GPx2	X68314	138319	TC repeats intron
glutathione peroxidase GPx2	X58295	138321	none found
glutathione peroxidase GPx3	X71973	138322	none found
glutathione peroxidase GPx4	AJ005277	603435	none found
glutathione peroxidase GPx5			

glutathione reductase	X15722	138300	two polymorphisms reported
N-methylpurine-DNA glycosylase	M74905	156565	none found
proliferating cell nuclear antigen	J04718	176740	none found
multidrug resistance associated protein	L05628	158343	none found
MRP1			
multidrug resistance associated protein	U83659	601107	none found
MRP2			
dihydrofolate reductase	J00140	126060	intronic polymorphism
dihydrofolate reductase	J00140	126060	2 RFLP's
thymidylate synthetase	X02308	188350	5' trinucleotide repeat
thymidylate synthetase	X02308	188350	tyr33his
thymidylate synthetase	X02308	188350	A->G 3'UTR
human cell adhesion protein SQM1	M33374	603842	none found
reduced folate carrier	U19720	600424	none found
RFC1			
thymidylate synthetase	X02308	188350	Triple tandem 5'end
thymidylate synthetase	X02308	188350	tyr33his
cytidine deaminase	L27943	123920	none found
folypolyglutamate synthetase FPGS	M98045	136510	none found
gamma-glutamyl hydrolase GGH	U55206	601509	none found
dihydropyrimidine	U09178	274270	165-BP DEL

dehydrogenase DPD	U09178	274270	ASP974VAL
dihydropyrimidine			
dehydrogenase DPD	U09178	274270	4-BP DEL 296 to 299 (TCAT)
dihydropyrimidine			
dehydrogenase DPD	U09178	274270	CYS29ARG
dihydropyrimidine			
dehydrogenase DPD	U09178	274270	1-BP DEL, 1897C Frameshift
dihydropyrimidine			
dehydrogenase DPD	U09178	274270	ARG886HIS
dihydropyrimidine			
dehydrogenase DPD	U09178	274270	Arg21Gln
dihydropyrimidine			
dehydrogenase DPD	U09178	274270	Val335Leu
dihydropyrimidine			
dehydrogenase DPD	U09178	274270	Glu386Ter
dihydropyrimidine			
dehydrogenase DPD	U09178	274270	deltaC1897
dihydropyrimidine			
dehydrogenase DPD	U09178	274270	Ser534Asn
dihydropyrimidine			
dehydrogenase DPD	U09178	274270	Ile543Val
dihydropyrimidine			
dehydrogenase DPD	U09178	274270	Val732Ile
dihydropyrimidine			
dehydrogenase DPD	M60527	125450	115-base pair deletion G to A
deoxycytidine kinase			glutamic acid for glycine
deoxycytidine kinase	M60527	125450	none found
glucosylceramide synthase	D50840	602874	

hypoxanthine-guanine phosphoribosyltransferase	M31642	308000	ILE132MET
hypoxanthine-guanine phosphoribosyltransferase	M31642	308000	ASP80VAL
hypoxanthine-guanine phosphoribosyltransferase	M31642	308000	ASP201GLY
hypoxanthine-guanine phosphoribosyltransferase	M31642	308000	1-BP INS frameshift
hypoxanthine-guanine phosphoribosyltransferase	M31642	308000	EX8DEL
hypoxanthine-guanine phosphoribosyltransferase	M31642	308000	LEU41PRO
hypoxanthine-guanine phosphoribosyltransferase	M31642	308000	24AA+
hypoxanthine-guanine phosphoribosyltransferase	M31642	308000	PHE74LEU
hypoxanthine-guanine phosphoribosyltransferase	M31642	308000	ASP194ASN
hypoxanthine-guanine phosphoribosyltransferase	M31642	308000	ASP193ASN
hypoxanthine-guanine phosphoribosyltransferase	M31642	308000	SER110LEU

phosphoribosyltransferase	M31642	308000	VAL179DEL
hypoxanthine-guanine phosphoribosyltransferase	M31642	308000	VAL130ASP
phosphoribosyltransferase	M31642	308000	ALA161SER
phosphoribosyltransferase	M31642	308000	SER104ARG
phosphoribosyltransferase	M31642	308000	PHE199VAL
phosphoribosyltransferase	M31642	308000	GLY70GLU
phosphoribosyltransferase	M31642	308000	GLY71ARG
phosphoribosyltransferase	M31642	308000	GLN108TER
phosphoribosyltransferase	M31642	308000	HIS203ASP
phosphoribosyltransferase	M31642	308000	ARG44LYS

ase hypoxanthine-guanine phosphoribosyltransfer	M31642	308000	ASP176TYR
ase hypoxanthine-guanine phosphoribosyltransfer	M31642	308000	2-BP DEL frameshift
ase hypoxanthine-guanine phosphoribosyltransfer	M31642	308000	1-BP DEL, TTA-TA frameshift
ase hypoxanthine-guanine phosphoribosyltransfer	M31642	308000	1-BP DEL, TTG-TG frameshift
ase hypoxanthine-guanine phosphoribosyltransfer	M31642	308000	40-BP DEL frameshift
ase hypoxanthine-guanine phosphoribosyltransfer	M31642	308000	G-to-A +5 intron 8 splice
ase hypoxanthine-guanine phosphoribosyltransfer	M31642	308000	ATAG-TTTG -4 intron 8+I29
ase hypoxanthine-guanine phosphoribosyltransfer	M31642	308000	GTAAGT-to- GTAAAT intron 7
ase hypoxanthine-guanine phosphoribosyltransfer	M31642	308000	AG-to-TG intron 1
ase hypoxanthine-guanine phosphoribosyltransfer	M31642	308000	PRO176LEU

hypoxanthine-guanine phosphoribosyltransfer ase	M31642	308000	ARG51GLY
hypoxanthine-guanine phosphoribosyltransfer ase	M31642	308000	ARG51TER
hypoxanthine-guanine phosphoribosyltransfer ase	M31642	308000	MET56THR
hypoxanthine-guanine phosphoribosyltransfer ase	M31642	308000	MET143LYS
hypoxanthine-guanine phosphoribosyltransfer ase	M31642	308000	ARG170TER
hypoxanthine-guanine phosphoribosyltransfer ase	M31642	308000	13-BP DEL, 5- PRIME UTR
hypoxanthine-guanine phosphoribosyltransfer ase	M31642	308000	EX2DEL
hypoxanthine-guanine phosphoribosyltransfer ase	M31642	308000	EX4-9DEL
hypoxanthine-guanine phosphoribosyltransfer ase	M31642	308000	EX6-9DEL
hypoxanthine-guanine phosphoribosyltransfer ase	M31642	308000	EX9DEL
hypoxanthine-guanine phosphoribosyltransfer ase	M31642	308000	1-BP INS G 207 frameshift

phosphoribosyltransferase	M31642	308000	EX2-3DUP	
hypoxanthine-guanine phosphoribosyltransferase	M31642	308000		THR168ILE
phosphoribosyltransferase	M31642	308000		GLY16SER
phosphoribosyltransferase	M31642	308000		GLY58ARG
phosphoribosyltransferase	M31642	308000		LEU78VAL
phosphoribosyltransferase	M31642	308000	EX6DEL	
phosphoribosyltransferase	M31642	308000	1-BP INS, T INS 14823	
phosphoribosyltransferase	M31642	308000		ASP52GLY
phosphoribosyltransferase	M31642	308000		GLY140ASP
phosphoribosyltransferase	M31642	308000		ASP194GLU

ase hypoxanthine-guanine phosphoribosyltransferase	M31642	308000	TYR153TER
ase hypoxanthine-guanine phosphoribosyltransferase	M31642	308000	Mnl I
ase hypoxanthine-guanine phosphoribosyltransferase	M31642	308000	Bam HI
ase hypoxanthine-guanine phosphoribosyltransferase	M31642	308000	54 (from ATG to CTG) resulting in the replacement of methionine with leucine val179gly
ase hypoxanthine-guanine phosphoribosyltransferase	M31642	308000	gly180arg
ase hypoxanthine-guanine phosphoribosyltransferase	M31642	308000	51 del 747 and 797 truncated protein
Bcl-2	M13994	151430	ACC-->GCC Ala43Thr
Bcl-2	M13994	151430	EcoRI polymorphism G to A exon 2
Bcl-2	M13994	151430	ASP294GLY
protein kinase C alpha	X52479	176960	none found
protein kinase C beta 1	X06318	176970	

protein kinase C delta	L07861	176977	none found	
protein kinase C mu	X75756	*****	none found	
protein kinase C theta	L01087	600448	none found	
protein kinase C zeta	L14283	176982	none found	
ecto-5'-nucleotidase (CD73)	X55740	129190	none found	
alkaline phosphatase	NM_000478	171760	ALA162THR	
alkaline phosphatase	NM_000478	171760	ARG54CYS	
alkaline phosphatase	NM_000478	171760	ASP277ALA	
alkaline phosphatase	NM_000478	171760	ARG54PRO	
alkaline phosphatase	NM_000478	171760	GLN190PRO	
alkaline phosphatase	NM_000478	171760	ALA16VAL	
alkaline phosphatase	NM_000478	171760	TYR419HIS	
alkaline phosphatase	NM_000478	171760	GLU174LYS	
alkaline phosphatase	NM_000478	171760	ASP361VAL	
alkaline phosphatase	NM_000478	171760	GLY317ASP	
alkaline phosphatase	NM_000478	171760	PHE310LEU	
alkaline phosphatase	NM_000478	171760	GLY439ARG	
alkaline phosphatase	NM_000478	171760	1-BP DEL, 1735T frameshift	

alkaline phosphatase	NM_0004	171760	ARG119HIS
78			
alkaline phosphatase	NM_0004	171760	GLY145VAL
78			
alkaline phosphatase	NM_0004	171760	ScrFI
78			
alkaline phosphatase	NM_0004	171760	BclI
78			
ribonucleotide	X59543	180410	SacI polymorphism
reductase M1 subunit			within intron IX
ribonucleotide	X59543	180410	TaqI
reductase M1 subunit			
ribonucleotide	X59618	180390	none found
reductase M2 subunit			
aminopeptidase A	L14721	138297	none found
signal transducer and	M97935	600555	none found
activator of			
transcription STAT1			
topoisomerase IIa	J04088	126430	AGA to AAA ARG486LYS
topoisomerase IIa	J04088	126430	deletion of 1320- Deletion of
topoisomerase I	J03250	126420	1322 Ala429
topoisomerase I	J03250	126420	Lys-797-->Asn
topoisomerase I	J03250	126420	Arg449Gln
topoisomerase I	J03250	126420	ASP533GLY
topoisomerase I	J03250	126420	ASP583GLY
topoisomerase I	J03250	126420	Asn722Ser
myeloperoxidase	X04876	254600	TaqI
myeloperoxidase	X04876	254600	C8089T ARG569TRP
myeloperoxidase	X04876	254600	TYR173CYS
			MET251THR

myeloperoxidase	X04876	254600	G to A (promoter)
myeloperoxidase	X04876	254600	KpnI
myeloperoxidase	X04876	254600	Dinucleotide Repeat
myeloperoxidase	X04876	254600	EcoRV
myeloperoxidase	X04876	254600	PstI
b3-tubulin	U47634	60266	none found
interleukin 6 (IL6)	M14584	147620	174G-C
interleukin 6 (IL6)	M14584	147620	CA repeat
interleukin 6 (IL6)	M14584	147620	NlaIII promoter
interleukin 6 (IL6)	M14584	147620	AT repeat
interleukin 6 (IL6)	M14584	147620	MspI
interleukin 6 (IL6)	M14584	147620	BglI
interleukin 6 (IL6)	M14584	147620	BglII
interferon alpha1 (IFNa1)	X02956	147660	none found
tyrosine kinase-type cell surface receptor	X03363	164870	VAL655ILE
HER2/ERBB2	X03363	164870	VAL654ILE
tyrosine kinase-type cell surface receptor	X02469	191170	CGC-CCC Arg72 Pro
HER2/ERBB2	X02469	191170	CCG-CTG Pro82Leu
tumor protein p53	X02469	191170	ATG-ACG Met133Thr
tumor protein p53	X02469	191170	cCAA-TAA Gln136Term
tumor protein p53	X02469	191170	cAGA-TGA Arg209Term
tumor protein p53	X02469	191170	aCCC-TCC Pro151Ser
tumor protein p53	X02469	191170	CCG-CTG Pro152Leu
tumor protein p53	X02469	191170	gCCC-TCC Pro219Ser
tumor protein p53	X02469	191170	cAAC-GAC Asn235Asp
tumor protein p53	X02469	191170	GGC-GTC Gly154Val

tumor protein p53	X02469	191170	ACA-ATA Thr256Ile
tumor protein p53	X02469	191170	CGC-CAC Arg175His
tumor protein p53	X02469	191170	CAT-CGT His193Arg
tumor protein p53	X02469	191170	tCGA-TGA Arg213Term
tumor protein p53	X02469	191170	gCGT-TGT Arg273Cys
tumor protein p53	X02469	191170	TGT-TAT Cys275Tyr
tumor protein p53	X02469	191170	tGAG-AAG Glu180Lys
tumor protein p53	X02469	191170	CGC-CAC Arg181His
tumor protein p53	X02469	191170	gCGC-TGC Arg181Cys
tumor protein p53	X02469	191170	cCGA-TGA Arg196Term
tumor protein p53	X02469	191170	TAT-TGT Tyr220Cys
tumor protein p53	X02469	191170	cTCT-ACT Ser227Thr
tumor protein p53	X02469	191170	AAC-AGC Asn235Ser
tumor protein p53	X02469	191170	CGA-CCA Arg306Pro
tumor protein p53	X02469	191170	cCAC-AAC His233Asn
tumor protein p53	X02469	191170	ATCc-ATG Ile251Met
tumor protein p53	X02469	191170	TCC-TTC Ser241Phe
tumor protein p53	X02469	191170	CGG-CAG Arg248Gln
tumor protein p53	X02469	191170	GGC-GAC Gly245Asp
tumor protein p53	X02469	191170	cGGC-AGC Gly245Ser
tumor protein p53	X02469	191170	cCGG-TGG Arg282Trp
tumor protein p53	X02469	191170	cGGC-TGC Gly245Cys
tumor protein p53	X02469	191170	cCGG-TGG Arg248Trp
tumor protein p53	X02469	191170	CTC-CCC Leu252Pro
tumor protein p53	X02469	191170	gGAA-AAA Glu258Lys
tumor protein p53	X02469	191170	CTG-CAG Leu257Gln
tumor protein p53	X02469	191170	CTG-CCG Leu265Pro
tumor protein p53	X02469	191170	gCGA-TGA Arg306Term
tumor protein p53	X02469	191170	gGTG-TTG Val272Leu
tumor protein p53	X02469	191170	CGT-CAT Arg273His
tumor protein p53	X02469	191170	GGA-GTA Gly325Val

tumor protein p53	X02469	191170	CCT-CTT Pro278Leu
tumor protein p53	X02469	191170	GAA-GCA Glu286Ala
tumor protein p53	X02469	191170	gCGC-TGC Arg337Cys
tumor protein p53	X02469	191170	CTG-CCG Leu344Pro
tumor protein p53	X02469	191170	ARG249SER
tumor protein p53	X02469	191170	VAL157PHE
tumor protein p53	X02469	191170	CYS242TYR
tumor protein p53	X02469	191170	1-BP INS, 151C frameshift
tumor protein p53	X02469	191170	2-BP DEL, frameshift
tumor protein p53	X02469	191170	CODONS 209-210
tumor protein p53	X02469	191170	1-BP INS, CODONS frameshift
tumor protein p53	X02469	191170	71-72
tumor protein p53	X02469	191170	LYS120TER
tumor protein p53	X02469	191170	ARG280THR
tumor protein p53	X02469	191170	PRO151THR
tumor protein p53	X02469	191170	LEU35PHE
tumor protein p53	X02469	191170	1-BP DEL, CODON
tumor protein p53	X02469	191170	257
tumor protein p53	X02469	191170	ALA138PRO
tumor protein p53	X02469	191170	1-BP DEL Codon frameshift
tumor protein p53	X02469	191170	178
tumor necrosis factor alpha (TNFa)	X01394	191160	LEU29SER
tumor necrosis factor alpha (TNFa)	X01394	191160	-1,031 T-->C
tumor necrosis factor alpha (TNFa)	X01394	191160	-863 C-->A
tumor necrosis factor alpha (TNFa)	X01394	191160	C-850T
tumor necrosis factor alpha (TNFa)	X01394	191160	G -238 A

tumor necrosis factor alpha (TNFa)	X01394	191160	G -376 A	
tumor necrosis factor alpha (TNFa)	X01394	191160	C to T, -857T	
tumor necrosis factor alpha (TNFa)	X01394	191160	-308 G/A	
tumor necrosis factor alpha (TNFa)	X01394	191160	NcoI	
tumor necrosis factor alpha (TNFa)	X01394	191160	C-ins 5'UTR of exon 1	ARG32TRP
tumor necrosis factor alpha (TNFa)	X01394	191160	G-376A	
2',5'-oligoadenylate synthetase 1 (OAS1)	NM_0061 87	164350	none found	
2',5'-oligoadenylate synthetase 2 (OAS2)	M87284	603350	none found	
2',5'-oligoadenylate synthetase 3 (OAS3)	*****	603351	none found	
excision repair protein ERCC1	M13194	126380	codon 118 C->T silent	
xeroderma pigmentosum complementation group A	D14533	278700	ILE132MET	
xeroderma pigmentosum complementation group A	D14533	278700	ASP80VAL	
xeroderma	D14533	278700	ASP201GLY	

pigmentosum complementation group A	D14533	278700	56 CCTTGA to FS20TER CCTTTGA	
xeroderma pigmentosum complementation group A	D14533	278700	EX8DEL	
xeroderma pigmentosum complementation group A	D14533	278700		LEU41PRO
xeroderma pigmentosum complementation group A	D14533	278700		24AA+
xeroderma pigmentosum complementation group A	D14533	278700		PHE74LEU
xeroderma pigmentosum complementation group A	D14533	278700		ASP194ASN
xeroderma pigmentosum complementation group A	D14533	278700		ASP193ASN

xeroderma pigmentosum complementation group A	D14533	278700	SER110LEU
xeroderma pigmentosum complementation group A	D14533	278700	3-BP DEL VAL179DEL
xeroderma pigmentosum complementation group A	D14533	278700	VAL130ASP
xeroderma pigmentosum complementation group A	D14533	278700	ALA161SER
xeroderma pigmentosum complementation group A	D14533	278700	SER104ARG
xeroderma pigmentosum complementation group A	D14533	278700	PHE199VAL
xeroderma pigmentosum complementation group A	D14533	278700	GLY70GLU
xeroderma pigmentosum complementation group A	D14533	278700	GLY71ARG

group A xeroderma pigmentosum complementation	D14533	278700	GLN108TER
group A xeroderma pigmentosum complementation	D14533	278700	HIS203ASP
group A xeroderma pigmentosum complementation	D14533	278700	ARG44LYS
group A xeroderma pigmentosum complementation	D14533	278700	ASP176TYR
group A xeroderma pigmentosum complementation	D14533	278700	2-BP DEL, GT DEL frameshift
group A xeroderma pigmentosum complementation	D14533	278700	1-BP DEL, TTA- frameshift TA
group A xeroderma pigmentosum complementation	D14533	278700	40-BP DEL, FS frameshift
group A xeroderma pigmentosum	D14533	278700	G+5A intron 8

complementation group A xeroderma pigmentosum complementation	D14533	278700	ATAG-TTTG intron 8	
group A xeroderma pigmentosum complementation	D14533	278700	GTAAGT-to- GTAAAT intron 7	
group A xeroderma pigmentosum complementation	D14533	278700	AG-to-TG last 2 nucleotides of intron 1	PRO176LEU
group A xeroderma pigmentosum complementation	D14533	278700		ARG51GLY
group A xeroderma pigmentosum complementation	D14533	278700		ARG51TER
group A xeroderma pigmentosum complementation	D14533	278700		MET56THR
group A xeroderma	D14533	278700		MET143LYS

pigmentosum complementation group A	D14533	278700	ARG170TER
xeroderma pigmentosum complementation group A			
xeroderma pigmentosum complementation group A	D14533	278700	13-BP DEL, 5- PRIME UTR
xeroderma pigmentosum complementation group A			
xeroderma pigmentosum complementation group A	D14533	278700	EX2DEL
xeroderma pigmentosum complementation group A			
xeroderma pigmentosum complementation group A	D14533	278700	EX4-9DEL
xeroderma pigmentosum complementation group A			
xeroderma pigmentosum complementation group A	D14533	278700	EX6-9DEL
xeroderma pigmentosum complementation group A			
xeroderma pigmentosum complementation group A	D14533	278700	EX9DEL
xeroderma pigmentosum complementation group A			
xeroderma pigmentosum complementation group A	D14533	278700	null allele
xeroderma pigmentosum complementation group A			

xeroderma pigmentosum complementation group A	D14533	278700	G insertion at about nucleotide 207	
xeroderma pigmentosum complementation group A	D14533	278700	INV/DEL, EX6-9	
xeroderma pigmentosum complementation group A	D14533	278700	duplication of exons 2 and 3 and deletion of intron 1	THR168ILE
xeroderma pigmentosum complementation group A	D14533	278700		GLY16SER
xeroderma pigmentosum complementation group A	D14533	278700		GLY58ARG
xeroderma pigmentosum complementation group A	D14533	278700		LEU78VAL
xeroderma pigmentosum complementation	D14533	278700	EX6DEL	

group A xeroderma pigmentosum complementation	D14533	278700	T insertion nucleotide at either nucleotide 14823 or 14824	ASP52GLY
group A xeroderma pigmentosum complementation	D14533	278700		
group A xeroderma pigmentosum complementation	D14533	278700		GLY140ASP
group A xeroderma pigmentosum complementation	D14533	278700		ASP194GLU
group A xeroderma pigmentosum complementation	D14533	278700		TYR153TER
group A metallothionein 1b	AH00151 0	156349	none found	
metallothionein 1e	M10942	156351	none found	
metallothionein 1f	M10943	156352	none found	
metallothionein 1g	J03910	156353	none found	
metallothionein 2a	NM_0059 53	156360	BamHI	
metallothionein 3	NM_0059 54	139255	none found	
asparagine synthetase	M27396	108370	none found	

ornithine decarboxylase 1 (ODC1)	M16650	165640	none found	
O6 alkylguanine-DNA alkyltransferase	M60761	156569	1034A>G	
O6 alkylguanine-DNA alkyltransferase	M60761	156569	1099C>T	
O6 alkylguanine-DNA alkyltransferase	M60761	156569	79G>T	
O6 alkylguanine-DNA alkyltransferase	M60761	156569	GGA to AGA gly160arg	
mismatch repair protein hMSH2	U03911	120435	PRO622LEU	
mismatch repair protein hMSH2	U03911	120435	splice variant DEL 50 CODONS	
mismatch repair protein hMSH2	U03911	120435	ARG406TER	
mismatch repair protein hMSH2	U03911	120435	HIS639TYR	
mismatch repair protein hMSH2	U03911	120435	3-BP DEL ASN596DEL	
mismatch repair protein hMSH2	U03911	120435	C1801T GLN601TER	
mismatch repair protein hMSH2	U03911	120435	ARG524PRO	
mismatch repair protein hMSH2	U03911	120435	1-BP DEL TGT705TT	
mismatch repair protein hMSH2	U03911	120435	22-BP INS 289 codon 97	
mismatch repair protein hMSH2	U03911	120435	GLY322ASP	

mismatch repair protein hMSH2	U03911	120435	A-943+3-T DEL Exon 5
mismatch repair protein hMSH2	U03911	120435	C>T at codon 389
mismatch repair protein hMSH2	U03911	120435	711bp CGA>TGA arg>ter
mismatch repair protein hMSH2	U03911	120435	C/T promoter
mismatch repair protein hMSH2	U03911	120435	CTT to TTT at phe>leu codon 390
mismatch repair protein hMSH2	U03911	120435	1-bp insertion in exon 12
mismatch repair protein hMSH2	U03911	120435	codon 888 del C
mismatch repair protein hMSH2	U03911	120435	T-to-C exon 13
cytochrome P450 aromatase (CYP19)	X13589	107910	ARG435CYS
cytochrome P450 aromatase (CYP19)	X13589	107910	CYS437TYR
cytochrome P450 aromatase (CYP19)	X13589	107910	splice donor 29 extra amino (GT>GC) of intron 6 acids
cytochrome P450 aromatase (CYP19)	X13589	107910	ARG375CYS
cytochrome P450 aromatase (CYP19)	X13589	107910	1-BP DEL, 408C frameshift
cytochrome P450 aromatase (CYP19)	X13589	107910	GT to AT exon and intron 3
cytochrome P450 aromatase (CYP19)	X13589	107910	G-1094 -A ARG365GLN
cytochrome P450 aromatase (CYP19)	X13589	107910	G-->A at Val80 silent

aromatase (CYP19)	X13589	107910	G-to-A Val370-to-Met
cytochrome P450			
aromatase (CYP19)	X13589	107910	(TTTA) _n in intron 5
cytochrome P450			
aromatase (CYP19)	X13589	107910	Arg264cys
cytochrome P450			
aromatase (CYP19)	M11050	138040	ASP641VAL
glucocorticoid receptor			
glucocorticoid receptor	M11050	138040	4-BP DEL 2 bases of the exon and the first 2 nucleotides of intron 6
			LEU753PHE
glucocorticoid receptor	M11050	138040	ILE747THR
glucocorticoid receptor	M11050	138040	CYS736SER
glucocorticoid receptor	M11050	138040	CYS736THR
glucocorticoid receptor	M11050	138040	ASN363SER
glucocorticoid receptor	M11050	138040	Base-pair deletion in 32 amino acid exon 9 deletion
			Q710X
glucocorticoid receptor	M11050	138040	L753F
glucocorticoid receptor	M11050	138040	trinucleotide Arg453 insertion
glucocorticoid receptor	M11050	138040	T insertion 1188 and frameshift 1189
glucocorticoid receptor	M11050	138040	A to G 3'-splice frameshift junction of intron G
			BcII
glucocorticoid receptor	M11050	138040	TthIII1
glucocorticoid receptor	M11050	138040	none found
glucocorticoid receptor	U25029	138040	

alpha glucocorticoid receptor	X03348	138040	none found	
beta multidrug resistance protein MDR1	X96395	171050		GLY185VAL
multidrug resistance protein MDR1	X96395	171050		Ser893Ala
multidrug resistance protein MDR1	X96395	171050	HindIII	
progesterone receptor insulin-like growth factor binding protein 2	M15716 X16302	264080 146731	EcoRI	
insulin-like growth factor binding protein 4	M62403	146733	none found	
multidrug resistance protein MDR2	NM_0003 92	601107	none found	
lipocortin 1/annexin 1	V00546	151690	none found	
androgen receptor	M20132	313700	PARTIAL DEL	
androgen receptor	M20132	313700		ARG773CYS
androgen receptor	M20132	313700		TRP717TER
androgen receptor	M20132	313700		VAL866MET
androgen receptor	M20132	313700		TRP794TER
androgen receptor	M20132	313700		LYS588TER
androgen receptor	M20132	313700		TYR761CYS
androgen receptor	M20132	313700		LYS882TER
androgen receptor	M20132	313700		ARG772CYS
androgen receptor	M20132	313700		ALA771THR
androgen receptor	M20132	313700		MET786VAL
androgen receptor	M20132	313700		VAL730MET
androgen receptor	M20132	313700	(CAG) ⁿ	
androgen receptor	M20132	313700		ARG773HIS

androgen receptor	M20132	313700	ARG607GLN
androgen receptor	M20132	313700	VAL865MET
androgen receptor	M20132	313700	VAL865LEU
androgen receptor	M20132	313700	ARG855HIS
androgen receptor	M20132	313700	ILE869MET
androgen receptor	M20132	313700	GLN60TER
androgen receptor	M20132	313700	5-KB DEL,EX E
androgen receptor	M20132	313700	5-KB DEL, EX F,G
androgen receptor	M20132	313700	ARG608LYS
androgen receptor	M20132	313700	ARG839HIS
androgen receptor	M20132	313700	ARG839CYS
androgen receptor	M20132	313700	THR877ALA
androgen receptor	M20132	313700	LEU676PRO
androgen receptor	M20132	313700	THR877SER
androgen receptor	M20132	313700	HIS874TYR
androgen receptor	M20132	313700	GLN902ARG
androgen receptor	M20132	313700	ALA721THR
androgen receptor	M20132	313700	SER647ASN
androgen receptor	M20132	313700	LEU707ARG
androgen receptor	M20132	313700	CYS579PHE
androgen receptor	M20132	313700	PHE582TYR
androgen receptor	M20132	313700	PRO546SER
androgen receptor	M20132	313700	GLU2LYS
androgen receptor	M20132	313700	MET780ILE
androgen receptor	M20132	313700	ARG846HIS
androgen receptor	M20132	313700	Insert of 69
androgen receptor	M20132	313700	nucleotides
androgen receptor	M20132	313700	LEU172TER
androgen receptor	M20132	313700	(CAA) _n
androgen receptor	M20132	313700	(GGN) _n
androgen receptor	M20132	313700	pro892ser

androgen receptor	M20132	313700	598 or 599 ter
androgen receptor	M20132	313700	Del T at 3286 frameshift
androgen receptor	M20132	313700	Gln798Glu
androgen receptor	M20132	313700	G214R
androgen receptor	M20132	313700	G Codon 210 A
androgen receptor	M20132	313700	G Codon 211 A
androgen receptor	M20132	313700	Arg615His
androgen receptor	M20132	313700	Arg752Gln
androgen receptor	M20132	313700	C>T within exon B silent
androgen receptor	M20132	313700	G2677A glu629arg
androgen receptor	M20132	313700	Stu I
androgen receptor	M20132	313700	arg726leu
androgen receptor	M20132	313700	del1893 frameshift
androgen receptor	M20132	313700	arg840his
androgen receptor	M20132	313700	Hind III
androgen receptor	M20132	313700	val 581 phe
androgen receptor	M20132	313700	MaeIII
androgen receptor	M20132	313700	CAG340TAG Gln>Ter
androgen receptor	M20132	313700	gly743val
androgen receptor	M20132	313700	HpaII
androgen receptor	M20132	313700	HhaI
androgen receptor	M20132	313700	G2314A ala>thr
clustrin/TRPM-2	M64722	185430	asp317 his
clustrin/TRPM-2	M64722	185430	codon 328 (G-->A) asp328asp
fos proto-oncogene	K00650	164810	T-->C transition in intron 2
myc proto-oncogene	V00568	190080	PRO59ALA
myc proto-oncogene	V00568	190080	PRO57SER
myc proto-oncogene	V00568	190080	ASN86THR
myc proto-oncogene	V00568	190080	GLU39ASP
bleomycin hydrolase	X92106	602403	1450A-G ILE443VAL

estrogen receptor 1 (ESR1)	M12674	133430	done	
estrogen receptor 2 (ESR2)	X99101	601663	done	
trefoil factor 1/sP2	X00474	113710		
Bcl-2 associated protein/bax	L22473	600040	1-BP INS Codons 38 to 41	
Bcl-2 associated protein/bax	L22473	600040	1-BP DEL Codons 38 to 41	
Bcl-2 associated protein/bax	L22473	600040	GLY67ARG	
Bcl-2 associated protein/bax	L22473	600040	7-BP DEL codons 38 to 41	
protein kinase C alpha	X52479	176960	ASP294GLY	
protein kinase C beta 1	X06318	176970	none found	
protein kinase C delta	L07861	176977	none found	
protein kinase C mu	X75756	*****	none found	
protein kinase C theta	L01087	600448	none found	
protein kinase C zeta	L14283	176982	none found	
insulin-like growth factor binding protein 1	NM_0005 96	146730	none found	
insulin-like growth factor binding protein	U62015	602369	none found	
insulin-like growth factor binding protein 3	NM_0005 98	146732	none found	
insulin-like growth factor binding protein 5	L27560	146734	none found	
insulin-like growth factor binding protein 6	M69054	146735	none found	
insulin-like growth factor binding protein 6	L19182	602867	none found	

factor binding protein 7				
interferon gamma	NM_0008	602376	none found	
receptor 2 (IFNGR2)	74			
interferon alpha	X77722	107450	none found	
receptor 1 (IFNAR1)				
interferon alpha	U68755	147569	Gln64Arg	
receptor 2 (IFNAR2)				
interferon beta1	V00546	147640	none found	
(IFNb1)				
interferon gamma	L07633	147570	CA repeat itron 1	
(IFNg)				
interferon gamma	L07633	147570	CGA to CAA Arg140Gln	
(IFNg)				
interferon gamma	L07633	147570	G5644A	
(IFNg)				
interferon gamma	J03143	107470	395C-A SER-TER	
receptor 1 (IFNGR1)				
interferon gamma	J03143	107470	1-BP DEL frameshift	
receptor 1 (IFNGR1)				
interferon gamma	J03143	107470	ILE87THR	
receptor 1 (IFNGR1)				
interferon gamma	J03143	107470	4-BP INS 104 to 107 frameshift	
receptor 1 (IFNGR1)				
interferon gamma	J03143	107470	IVS3	
receptor 1 (IFNGR1)				
interferon gamma	J03143	107470	4-BP DEL truncated	
receptor 1 (IFNGR1)			protein	
interferon gamma	J03143	107470	Val14Met	
receptor 1 (IFNGR1)				
interferon gamma	J03143	107470	TaqI	
receptor 1 (IFNGR1)				

interferon omegal (IFNw1)	X02669	147553	none found
interleukin 1 alpha (IL1a)	M15329	147760	C to T -889
interleukin 1 alpha (IL1a)	M15329	147760	Dinucleotide repeat
interleukin 1 alpha (IL1a)	M15329	147760	46 bp tandem repeat intron 6
interleukin 1 beta (IL1b)	K02770	147720	TaqI
interleukin 1 beta (IL1b)	K02770	147720	+5887 C --> T
interleukin 1 beta (IL1b)	K02770	147720	position -511
interleukin 1 beta (IL1b)	K02770	147720	exon 5 (position +3953)
interleukin 1 beta (IL1b)	K02770	147720	Asp106Asn
interleukin 1 receptor (IL-1R)	M27492	147810	PstI
interleukin 10 (IL10)	M57627	124092	G -1082 A
interleukin 10 (IL10)	M57627	124092	C-to-A 571
interleukin 10 (IL10)	M57627	124092	A-597 C
interleukin 10 (IL10)	M57627	124092	T -824 C
interleukin 10 (IL10)	M57627	124092	second dinucleotide repeat
interleukin 10 (IL10)	M57627	124092	A -592 C
interleukin 10 (IL10)	M57627	124092	2 CA repeat
interleukin 10 receptor alpha (IL-10Ra)	U00672	146933	none found
interleukin 11 (IL11)	X58377	147681	5' dinucleotide

interleukin 12a (IL12a)	M65271	161560	repeat none found
interleukin 12b (IL12b)	M65272	161561	4.4-KB DEL
interleukin 13 (IL13)	X69079	147683	none found
interleukin 15 (IL15)	U14407	600554	none found
interleukin 15 receptor alpha (IL-15Ra)	U31628	601070	none found
interleukin 16 (IL16)	NM_0045 13	603035	none found
interleukin 18 (IL18)	*****	600953	none found
interleukin 2 (IL2)	X01586	147680	-330
interleukin 2 (IL2)	X01586	147680	166
interleukin 2 (IL2)	X01586	147680	Dinucleotide Repeat
interleukin 2 (IL2)	X01586	147680	AUUUA motif deleted
interleukin 2 receptor alpha (IL-2Ra)	X01057	147730	4-BP DEL 60 to 64 frameshift
interleukin 2 receptor alpha (IL-2Ra)	X01057	147730	TaqI
interleukin 2 receptor beta (IL-2Rb)	M26062	146710	CA repeat
interleukin 2 receptor gamma (IL-2Rg)	D11086	308380	LYS97TER
interleukin 2 receptor gamma (IL-2Rg)	D11086	308380	ARG267TER
interleukin 2 receptor gamma (IL-2Rg)	D11086	308380	SER286TER
interleukin 2 receptor gamma (IL-2Rg)	D11086	308380	CYS62TER
interleukin 2 receptor gamma (IL-2Rg)	D11086	308380	GLY114ASP

interleukin 2 receptor gamma (IL-2Rg)	D11086	308380	G-to-A first position of intron 3	ILE153ASN
interleukin 2 receptor gamma (IL-2Rg)	D11086	308380		
interleukin 2 receptor gamma (IL-2Rg)	D11086	308380		LEU271GLN
interleukin 2 receptor gamma (IL-2Rg)	D11086	308380	9-BP DUP	GLN-HIS-TRP INS
interleukin 2 receptor gamma (IL-2Rg)	D11086	308380		CYS115ARG
interleukin 2 receptor gamma (IL-2Rg)	D11086	308380		ARG285GLN
interleukin 2 receptor gamma (IL-2Rg)	D11086	308380		ARG222CYS
interleukin 2 receptor gamma (IL-2Rg)	D11086	308380	690-691 hotspot	
interleukin 3 (IL3)	M20137	147740	none found	
interleukin 3 alpha receptor (IL-3aR)	M74782	308385	none found	
interleukin 4 (IL4)	M13982	147780	C-589T	
interleukin 4 (IL4)	M13982	147780	Dinucleotide Repeat intron 2	
interleukin 4 (IL4)	M13982	147780	-285 C-T	
interleukin 4 receptor (IL-4R)	X52425	147781	-81 A-G	GLN576ARG
interleukin 4 receptor (IL-4R)	X52425	147781		ILE50VAL
interleukin 4 receptor (IL-4R)	X52425	147781		S503P
interleukin 5 (IL5)	X04688	147850	none found	

interleukin 5 receptor alpha (IL-5Ra)	M96652	147851	Dinucleotide repeat	
interleukin 6 receptor (IL-6R) (20)	M20566	147880	dinucleotide (CA)	
interleukin 7 (IL7)	J04156	146660	none found	
interleukin 7 receptor (IL-7R)	M29696	146661		THR66ILE
interleukin 7 receptor (IL-7R)	M29696	146661		ILE138VAL
interleukin 7 receptor (IL-7R)	M29696	146661	AG-to-AA splice junction intron 4	
interleukin 7 receptor (IL-7R)	M29696	146661		trp217 to ter
interleukin 8 (IL8)	M26383	146930	HindIII	
interleukin 8 receptor alpha (IL-8Ra)	M68932	146929	none found	
interleukin 8 receptor beta (IL-8Rb)	M94582	146928	none found	
interleukin 9 (IL9)	X17543	146931	Dinucleotide repeat	
interleukin 9 receptor (IL-9R)	M84747	300007	none found	
interleukin receptor 11 alpha (IL-11a)	U32324	600939	none found	
interleukin receptor 12 beta (IL-12b)	U03187	601604		GLN32TER
interleukin receptor 12 beta (IL-12b)	U03187	601604		GLN376TER
interleukin receptor 12 beta (IL-12b)	U03187	601604	409-549DEL frameshift	
interleukin receptor 12 beta2 (IL-12b2)	U03187	601642	none found	

interleukin receptor 13 alpha (IL-13a)	S80963	300119	none found
interleukin receptor 13 alpha2 (IL-13a2)	X95302	300130	none found
lipocortin 2/annexin 2	D00017	151740	none found
lipocortin 3/annexin 3	M20560	106490	tandem repeat TAAA
lipocortin 3/annexin 3	M20560	106490	SalI
lipocortin 3/annexin 3	M20560	106490	BglII
lipocortin 5/annexin 5	NM_0011 54	131230	EcoRI
lipocortin 5/annexin 5	NM_0011 54	131230	PvuII
lipocortin 7/annexin 7 (splice variant 1)	NM_0040 34	186360	none found
lipocortin 7/annexin 7 (splice variant 2)	NM_0011 56	186360	none found
trefoil factor 2/TFF2	X51698	182590	25 bp tandem repeat
trefoil factor 3/sP2	L08044	600633	none found

Table 19. Identified
Variances in Genes or
Related Pathways
involved in
Neurological or
Psychiatric Disease

Nicotinic, Cholinergic receptor beta 1	X14830	100710	LEU263MET
Nicotinic, Cholinergic receptor beta 1	X14830	100710	VAL266MET

Nicotinic, Cholinergic receptor, muscle d	X55019	100720	none found	
Nicotinic, Cholinergic receptor epsilon polypeptide	X66403	100725	ARG147LEU	
Nicotinic, Cholinergic receptor epsilon polypeptide	X66403	100725	ARG64TER	
Nicotinic, Cholinergic receptor epsilon polypeptide	X66403	100725	LEU269PHE	
Nicotinic, Cholinergic receptor epsilon polypeptide	X66403	100725	PRO121LEU	
Nicotinic, Cholinergic receptor epsilon polypeptide	X66403	100725	THR264PRO	
Nicotinic, Cholinergic receptor, muscle g	NM_0051 99	100730	none found	
Acetylcholinesterase/A CHE	M55040	100740	1431 C/T 446 silent	
Acetylcholinesterase/A CHE	M55040	100740	408 G/C arg561pro	
Acetylcholinesterase/A CHE	M55040	100740	HIS322ASN	
adenosine deaminase	NM_0000 22	102700	LYS80ARG	
adenosine deaminase	NM_0000 22	102700	ARG101TRP	
adenosine deaminase	NM_0000 22	102700	ARG101GLN	

adenosine deaminase NM_000022	102700	ARG211HIS
adenosine deaminase NM_000022	102700	LEU304ARG
adenosine deaminase NM_000022	102700	ALA329VAL
adenosine deaminase NM_000022	102700	ALA39VAL
adenosine deaminase NM_000022	102700	3.25-KB DEL
adenosine deaminase NM_000022	102700	PRO297GLN
adenosine deaminase NM_000022	102700	ARG76TRP
adenosine deaminase NM_000022	102700	ARG149GLN
adenosine deaminase NM_000022	102700	PRO274LEU
adenosine deaminase NM_000022	102700	LEU107PRO
adenosine deaminase NM_000022	102700	ARG211CYS
adenosine deaminase NM_000022	102700	ALA215THR
adenosine deaminase NM_000022	102700	GLY216ARG
adenosine deaminase NM_000022	102700	IVS3AS, A-G, -2 EX4DEL
adenosine deaminase NM_000022	102700	ARG156CYS
adenosine deaminase NM_000022	102700	SER291LEU

adenosine deaminase NM_000022	102700	IVS10AS, G-A, -34	
adenosine deaminase NM_000022	102700		ASP8ASN
adenosine deaminase NM_000022	102700	IVS2DS, G-A, +1	
adenosine deaminase NM_000022	102700	7-BP INS, IVS8AS	
adenosine deaminase NM_000022	102700	IVS1DS, G-C, +1	
adenosine deaminase NM_000022	102700		GLY74VAL
adenosine deaminase NM_000022	102700	IVS5DS, G-A, +1, EX5 DEL 116-BP DEL	
adenosine deaminase NM_000022	102700		LEU152MET
adenosine deaminase NM_000022	102700		THR233ILE
adenosine deaminase NM_000022	102700		TYR97CYS
adenosine deaminase NM_000022	102700		LEU106VAL
adenosine deaminase NM_000022	102700		G74C
adenosine deaminase NM_000022	102700		V129M
adenosine deaminase NM_000022	102700		G140E
adenosine deaminase NM_000022	102700		R149W

adenosine deaminase NM_000022	102700	Q199P
adenosine deaminase NM_000022	102700	462delG
adenosine deaminase NM_000022	102700	E337del
adenosine deaminase NM_000022	102700	tetranucleotide repeat
adenosine deaminase NM_000022	102700	Q3X
adenosine deaminase NM_000022	102700	R142Q
adenosine deaminase NM_000022	102700	R142X
adenosine deaminase NM_000022	102700	PstI
adenosine deaminase NM_000022	102700	G to A at the invariant 5' GT of intron 7
adenosine deaminase NM_000022	102700	Glu 217 Lys
adenosine deaminase NM_000022	102700	del exon 7
adenosine deaminase NM_000022	102700	Apa I
Adenosine A1 Receptor; Adora1/G protein-coupled	102775	1777C/A
Adenosine A1 Receptor; Adora1/G protein-coupled	102775	1827C/T

Adenosine A1 Receptor; Adora1/G protein-coupled	L22214	102775	1904C/T
Adenosine A1 Receptor; Adora1/G protein-coupled	L22214	102775	2126G/T
Adenosine A1 Receptor; Adora1/G protein-coupled	L22214	102775	2294insT
Adenosine A1 Receptor; Adora1/G protein-coupled	L22214	102775	267 + 275C/T
Adenosine A1 Receptor; Adora1/G protein-coupled	L22214	102775	2776C/T
Adenosine A1 Receptor; Adora1/G protein-coupled	L22214	102775	2777del36
Adenosine A1 Receptor; Adora1/G protein-coupled	L22214	102775	2819T/G
Adenosine A1 Receptor; Adora1/G protein-coupled	L22214	102775	805T/G
Adenosine A1 Receptor; Adora1/G protein-coupled	L22214	102775	48T/A
Adenosine A1 Receptor; Adora1/G protein-coupled	L22214	102775	716T/G
Adenosine A2	X68486	102776	1083C/T

Receptor; Adora2a/G protein-coupled Adenosine A2	X68486	102776	405C/T	
Receptor; Adora2a/G protein-coupled Adenosine A2	X68486	102776	432C/T	
Receptor; Adora2a/G protein-coupled Adenosine A2	X68486	102776		Gly-340-Ser
Receptor- like/ADORA2L1 adenylate-cyclase activating polypeptide 1	*****	102777	none found	
receptor/ADCYAP1R1 alpha-2a-adrenergic receptor; ADRA2A	D17516	102981	none found	
alpha-2a-adrenergic receptor; ADRA2A	M18415	104210	-1291	
alpha-2a-adrenergic receptor; ADRA2A	M18415	104210	DraI	
alpha-2a-adrenergic receptor; ADRA2A	M18415	104210	HhaI	
alpha-2a-adrenergic receptor; ADRA2A	M18415	104210	MspI promoter	
alpha-1a-adrenergic receptor; ADRA1A	M76446	104219	none found	
alpha-1b-adrenergic receptor; ADRA1B	L31773	104220	none found	
alpha-1c-adrenergic	D25235	104221	PstI	

receptor; ADRA1C	M76446	104222	none found	
alpha-1d-adrenergic				
receptor; ADRA1D	J03853	104250	(CA)n	
alpha-2c-adrenergic				
receptor; ADRA2C	AF005900	104260	none found	
alpha-2b-adrenergic				
receptor; ADRA2B	NM_0000	104311	IVS8AS, G-T, -1,	
presenilin 1	21		EX9DEL	
presenilin 1	NM_0000	104311	1-BP DEL, G	
presenilin 1	21			
presenilin 1	NM_0000	104311	intron 3' to exon 8	
presenilin 1	21			
presenilin 1	NM_0000	104311	T/G intron 9	
presenilin 1	21			
presenilin 1	NM_0000	104311	HIS163ARG	
presenilin 1	21			
presenilin 1	NM_0000	104311	ALA246GLU	
presenilin 1	21			
presenilin 1	NM_0000	104311	ALA426PRO	
presenilin 1	21			
presenilin 1	NM_0000	104311	ARG278THR	
presenilin 1	21			
presenilin 1	NM_0000	104311	CYS410TYR	
presenilin 1	21			
presenilin 1	NM_0000	104311	GLU120ASP	
presenilin 1	21			
presenilin 1	NM_0000	104311	GLU280ALA	
presenilin 1	21			
presenilin 1	NM_0000	104311	GLU280GLY	
presenilin 1	21			

presenilin 1	NM_000021	104311	Glu318Gly
presenilin 1	NM_000021	104311	gly378glu
presenilin 1	NM_000021	104311	HIS163TYR
presenilin 1	NM_000021	104311	LEU250SER
presenilin 1	NM_000021	104311	Leu262Phe
presenilin 1	NM_000021	104311	Leu282Arg
presenilin 1	NM_000021	104311	LEU286VAL
presenilin 1	NM_000021	104311	lys123glu
presenilin 1	NM_000021	104311	MET139VAL
presenilin 1	NM_000021	104311	MET146ILE
presenilin 1	NM_000021	104311	MET146LEU
presenilin 1	NM_000021	104311	MET146VAL
presenilin 1	NM_000021	104311	PRO267SER
presenilin 1	NM_000021	104311	Pro436Gln
presenilin 1	NM_000021	104311	Ser169Leu
Human cerebrovascular	M16765	104760	

[illegible]

E/APOE	41	creates 2 abnormally spliced mRNA forms
apolipoprotein E/APOE	NM_000041	C305G Proline84Arginine
apolipoprotein E/APOE	NM_000041	C460A Arginine136Serine
apolipoprotein E/APOE	NM_000041	C478T Arg142142Cys142
apolipoprotein E/APOE	NM_000041	C487T Arginine145Cysteine
apolipoprotein E/APOE	NM_000041	C526T Arginine158Cysteine
apolipoprotein E/APOE	NM_000041	C736T Arginine228Cysteine
apolipoprotein E/APOE	NM_000041	C805G Arg251251Gly251
apolipoprotein E/APOE	NM_000041	G144deletion Leucine60Termination Codon (frameshift)
apolipoprotein E/APOE	NM_000041	G349A Ala9999Thr99
apolipoprotein E/APOE	NM_000041	G434A Gly127127Asp127
apolipoprotein E/APOE	NM_000041	G455A Arginine134Glutamine
apolipoprotein E/APOE	NM_000041	G488A Arginine145Histidine
apolipoprotein E/APOE	NM_000041	G568C Ala152Proline

apolipoprotein E/APOE	NM_000041	107741	G61A Glutamic Acid3Lysine
apolipoprotein E/APOE	NM_000041	107741	G683A Tryptophan210 Termination Codon
apolipoprotein E/APOE	NM_000041	107741	G725A Arg224224Gln224
apolipoprotein E/APOE	NM_000041	107741	G875A Arginine274His tidine
apolipoprotein E/APOE	NM_000041	107741	G91A Glutamic Acid13Lysine
apolipoprotein E/APOE	NM_000041	107741	GAG-GAG844- Glu244/Glu245 849AAG-AAG 244- 245Lys244/Lys 245
apolipoprotein E/APOE	NM_000041	107741	T137C Leucine28Proline
apolipoprotein E/APOE	NM_000041	107741	T388C Cysteine112Arg inine
apolipoprotein E/APOE	NM_000041	107741	T761A Valine236Glutamic Acid
Aromatic L-Amino Acid	M76180	107930	SspI
Decarboxylase/AADC/ dopa decarboxylase			
Benzodiazepine receptor, peripheral type	NM_000714	109610	none found
beta-1-adrenergic receptor; Adrb1	J03019	109630	Bgl I.
beta-1-adrenergic	J03019	109630	C1165G ARG389GLY

receptor; Adrb1 beta-adrenergic receptor kinase 1/BARK1	NM_001619	109635	none found	
Beta-Adrenergic Receptor Kinase 2; Adrbk2	X69117	109636	none found	
Beta-2-Adrenergic Receptor; Adrb2	M15169	109690	Fnu4HI	
Beta-2-Adrenergic Receptor; Adrb2	M15169	109690	A-->G -1343	
Beta-2-Adrenergic Receptor; Adrb2	M15169	109690	C-->G -468	
Beta-2-Adrenergic Receptor; Adrb2	M15169	109690	G-->A -1023	
Beta-2-Adrenergic Receptor; Adrb2	M15169	109690	G-->A -654	
Beta-2-Adrenergic Receptor; Adrb2	M15169	109690	T-->A -1429	
Beta-2-Adrenergic Receptor; Adrb2	M15169	109690	T-->C -20	
Beta-2-Adrenergic Receptor; Adrb2	M15169	109690	T-->C -367	
Beta-2-Adrenergic Receptor; Adrb2	M15169	109690	T-->C -47	
Beta-2-Adrenergic Receptor; Adrb2	M15169	109690		ARG16GLY
Beta-2-Adrenergic Receptor; Adrb2	M15169	109690		GLN27GLU
Beta-2-Adrenergic Receptor; Adrb2	M15169	109690		Thr164Ile

Beta-2-Adrenergic Receptor; Adrb2	M15169	109690	val 34 met
Beta-3-Adrenergic Receptor; Adrb3	X70811	109691	intron 1 g1856t
Beta-3-Adrenergic Receptor; Adrb3	X70811	109691	TRP64ARG
serotonin 5-HT receptors 5-HT1A, G	X57829	109760	RsaI
protein-coupled bradykinin receptor B2/BDKRB2 G	NM_000623	113503	-143C/T
protein-coupled bradykinin receptor B2/BDKRB2 G	NM_000623	113503	-412C/G
protein-coupled bradykinin receptor B2/BDKRB2 G	NM_000623	113503	-536C/T
protein-coupled bradykinin receptor B2/BDKRB2 G	NM_000623	113503	-640T/C
protein-coupled bradykinin receptor B2/BDKRB2 G	NM_000623	113503	-649insG
protein-coupled bradykinin receptor B2/BDKRB2 G	NM_000623	113503	-704C/T
protein-coupled bradykinin receptor B2/BDKRB2 G	NM_000623	113503	-78C/T
protein-coupled bradykinin receptor	NM_0006	113503	-845C/T

B2/BDKRB2 G	23				
protein-coupled					
bradykinin receptor				9 bp de (-)21-29	
B2/BDKRB2 G	NM_0006 23	113503			
protein-coupled					
bradykinin receptor				C>T promoter 54	
B2/BDKRB2 G	NM_0006 23	113503			
protein-coupled				repeat 3'UTR	
bradykinin receptor					
B2/BDKRB2 G	NM_0006 23	113503			
protein-coupled				tandem repeat near promoter	
bradykinin receptor					
B2/BDKRB2 G	NM_0006 23	113503			R14C
protein-coupled					
bradykinin receptor					
B2/BDKRB2 G	NM_0006 23	113503			
protein-coupled					
bradykinin receptor					
B2/BDKRB2 G	NM_0006 23	113503			T21M
protein-coupled					
L-type voltage					
dependent calcium				none found	
channel alpha 1C					
subunit/CACNA1C					
L-type voltage					ARG1086HIS
dependent calcium					
channel alpha 1S					
subunit/CACNA1S					
L-type voltage					ARG1239GLY
dependent calcium					
channel alpha 1S					

subunit/CACNA1S				
L-type voltage dependent calcium channel alpha 1S	NM_000069	114208		ARG1239HIS
subunit/CACNA1S				
L-type voltage dependent calcium channel alpha 1S	NM_000069	114208		ARG528HIS
subunit/CACNA1S				
calpain, large polypeptide L3/CAPN3	NM_000070	114240		ARG572GLN
calpain, large polypeptide L3/CAPN3	NM_000070	114240		ARG110TER
calpain, large polypeptide L3/CAPN3	NM_000070	114240		ARG769GLN
calpain, large polypeptide L3/CAPN3	NM_000070	114240		PRO319LEU
calpain, large polypeptide L3/CAPN3	NM_000070	114240		SER86PHE
cannabinoid receptor 1/G protein-coupled/CNR1	NM_001840	114610	1359G-->A silent	
Catechol-O-Methyltransferase	M58525	116790	186C > T at exon 3	
Catechol-O-Methyltransferase	M58525	116790	408C > G at exon 4	

SD-144141.1

Catechol-O-Methyltransferase	M58525	116790	472G > A at exon 4	
Catechol-O-Methyltransferase	M58525	116790	597G > A at exon 5	
Catechol-O-Methyltransferase	M58525	116790	821-827insC at the 3'	
Catechol-O-Methyltransferase	M58525	116790	BglI	
Catechol-O-Methyltransferase	M58525	116790	C256G silent	
Catechol-O-Methyltransferase	M58525	116790	G/A1947	
Catechol-O-Methyltransferase	M58525	116790	MspI	
Catechol-O-Methyltransferase	M58525	116790	NlaIII	
Catechol-O-Methyltransferase	M58525	116790	val-108-met	
Catechol-O-Methyltransferase	M58525	116790	Val158-->Met	
Methyltransferase B/b-aCTSBmyloid precursor protein secretase/CTSB	M14221	116810	10-bp insertion in the 3'-UT	
cathepsin B/b-aCTSBmyloid precursor protein secretase/CTSB	M14221	116810	CYS26ARG	
cathepsin B/b-aCTSBmyloid precursor protein	M14221	116810	EcoRI	

SD-14141.1

secretase/CTSB	M14221	116810	TaqI	
cathepsin B/b-aCTSBmyloid precursor protein				
secretase/CTSB	L13605	118444	GLY21ARG	
Cholecystokinin A receptor/CCKAR	L13605	118444	VAL365ILE	
Cholecystokinin A receptor/CCKAR	L08112	118445	1550 G-->A Val125-->Ile	
Cholecystokinin B receptor/CCKBR	L08112	118445	CAT 207 CAC His207His	
Cholecystokinin B receptor/CCKBR	L08112	118445	Arg215His	
Cholecystokinin B receptor/CCKBR	L08112	118445	Val138Met	
plasma cholesterol ester transfer protein/CETP	NM_000078	118470	A1503G	
plasma cholesterol ester transfer protein/CETP	NM_000078	118470	G-A splice junction alternative splice	
plasma cholesterol ester transfer protein/CETP	NM_000078	118470	G1696A	
plasma cholesterol ester transfer protein/CETP	NM_000078	118470	C-T transition in intron 12	
plasma cholesterol ester transfer protein/CETP	NM_000078	118470	EcoNI	

SD-144141.1

protein/CETP plasma cholesterol ester transfer	NM_0000 78	118470	G-->A intron 14
protein/CETP plasma cholesterol ester transfer	NM_0000 78	118470	G-A transition in intron 15
protein/CETP plasma cholesterol ester transfer	NM_0000 78	118470	G1533A
protein/CETP plasma cholesterol ester transfer	NM_0000 78	118470	INS T alternative (intron/exon14) splice
protein/CETP plasma cholesterol ester transfer	NM_0000 78	118470	StuI
protein/CETP plasma cholesterol ester transfer	NM_0000 78	118470	T-->G tyr57stop
protein/CETP plasma cholesterol ester transfer	NM_0000 78	118470	TaqIA
protein/CETP plasma cholesterol ester transfer	NM_0000 78	118470	TaqIB in intron 1
protein/CETP plasma cholesterol ester transfer	NM_0000 78	118470	268 Arg-- >STOP
protein/CETP plasma cholesterol ester transfer	NM_0000 78	118470	Asp 442 to Gly

SD-144141.1

plasma cholesterol ester transfer protein/CETP	NM_0000 78	118470	ASP442GLY
plasma cholesterol ester transfer protein/CETP	NM_0000 78	118470	G181X
plasma cholesterol ester transfer protein/CETP	NM_0000 78	118470	I405V
plasma cholesterol ester transfer protein/CETP	NM_0000 78	118470	Lys309-Stop
plasma cholesterol ester transfer protein/CETP	NM_0000 78	118470	R451Q
plasma cholesterol ester transfer protein/CETP	NM_0000 78	118470	Val421-Ile
Choline acetyltransferase/CHA T	NM_0030 55	118490	none found
Cholinergic Receptor, Muscarinic, 2; CHRM2	U19800	118493	none found
Cholinergic Receptor, Muscarinic, 3; CHRM3	U29589	118494	none found
Cholinergic Receptor, Muscarinic, 4; CHRM4	M16405	118495	SstI
Cholinergic Receptor, Muscarinic, 5; CHRM5	AF026263	118496	none found
Nicotinic, Cholinergic receptor alpha 2	U62431	118502	none found

SD-14:141.1

Page 1257

Nicotinic, Cholinergic receptor alpha 3	X53559	118503	none found	
Nicotinic, Cholinergic receptor alpha 4	U62433	118504	3-BP INS, 776GCT	
Nicotinic, Cholinergic receptor alpha 4	U62433	118504	CfoI exon 5	
Nicotinic, Cholinergic receptor alpha 4	U62433	118504	Dinucleotide intron 1	
Nicotinic, Cholinergic receptor alpha 4	U62433	118504	fokI	
Nicotinic, Cholinergic receptor alpha 4	U62433	118504	PvuII	
Nicotinic, Cholinergic receptor alpha 4	U62433	118504	SER-TER	
Nicotinic, Cholinergic receptor alpha 4	U62433	118504	SER248PHE	
Nicotinic, Cholinergic receptor alpha 5	M83712	118505	none found	
Nicotinic, Cholinergic receptor beta 2	Y08415	118507	none found	
Nicotinic, Cholinergic receptor beta 3	X67513	118508	none found	
Nicotinic, Cholinergic receptor beta 4	X68275	118509	none found	
Cholinergic Receptor, Muscarinic, 1; CHRM1	X15263	118510	none found	
Nicotinic, Cholinergic receptor alpha 7	U40583	118511	none found	
ciliary neurotrophic factor receptor/CNTRF	NM_0018 42	118946	none found	
Corticotropin releasing	U16273	122561	none found	

SD-14141.1

hormone receptor 1				
diazepam binding	M15887	125950	none found	
inhibitor/DBI				
Human dihydrofolate	J00140	126060		
reductase gene				C/T Isoleucine49
Dopamine Receptor D1	X58987	126449	141 C ins/del	
Dopamine Receptor D2	X51362	126450	A241G	
Dopamine Receptor D2	X51362	126450	NcoI RFLP	
Dopamine Receptor D2	X51362	126450	TaqI A, TaqI B,	
Dopamine Receptor D2	X51362	126450	TaqI D, and (CA) _n	
			STRP	
Dopamine Receptor D2	X51362	126450	Serine	
			311Cysteine	
Dopamine Receptor D3	U32499	126451	exonic Ball	
			polymorphism	
Dopamine Receptor D3	U32499	126451	intronic MspI	
			polymorphism	
Dopamine Receptor D3	U32499	126451	Serine9Glycine	
Dopamine Receptor D4	L12398	126452	12 bp	
			duplication/deletion	
			in exon 1	
Dopamine Receptor D4	L12398	126452	12 bp tandem repeat	
			in extracellular N-	
			terminal part of	
			receptor	
Dopamine Receptor D4	L12398	126452	12 bp VNTR in exon	
			1	
Dopamine Receptor D4	L12398	126452	48 bp VNTR in exon	
			3	
Dopamine Receptor D4	L12398	126452	48 bp VNTR in exon	

Dopamine Receptor D4	L12398	126452	3 48 bp VNTR in exon 3
Dopamine Receptor D4	L12398	126452	48 bp VNTR in third cytoplasmic loop
Dopamine Receptor D4	L12398	126452	exon 1 -- nondeleted sequence in 13bp deletion site
Dopamine Receptor D4	L12398	126452	exon 3 (48 bp repeat)
Dopamine Receptor D4	L12398	126452	exon 3 (position 194) -- common valine producing T at glycine subst site
Dopamine Receptor D4	L12398	126452	poly G in intron 1
Dopamine Receptor D4	L12398	126452	SmaI cutting site (bands of 413bp and 302bp) in 5' noncoding region
Dopamine Receptor D4	L12398	126452	SmaI RFLP in 5' noncoding region
Dopamine Receptor D5	M67439	126453	(TC) _n
Dopamine Receptor D5	M67439	126453	dinucleotide repeat
Dopamine Receptor D5	M67439	126453	poly (CT/GT/GA) _n
Dopamine Receptor D5	M67439	126453	T978C P326P
Dopamine Receptor D5	M67439	126453	transmembrane L88F domain II
Dopamine Transporter/ DAT1	L24178	126455	40-bp VNTR in the 3'-untranslated
Dopamine Transporter/ DAT1	L24178	126455	5' TaqI RFLP

Dopamine Transporter/ DAT1	L24178	126455	9-repeat allele
estrogen receptor 1 (ESR1)	M12674	133430	RFLP (PssI enzyme)
estrogen receptor 1 (ESR1)	M12674	133430	RFLP (PvuII enzyme) none found
Solute Carrier Family 1, Member 1; Slc1a1	U08989	133550	none found
Gamma-Aminobutyric Acid Receptor, Alpha- 2; Gabra2	S62907	137140	none found
Gamma-Aminobutyric Acid Receptor, Alpha- 4; Gabra4	U30461	137141	none found
Gamma-Aminobutyric Acid Receptor, Alpha- 5; Gabra5	L08485	137142	Dinucleotide repeat
Gamma-Aminobutyric Acid Receptor, Alpha- 6; Gabra6	S81944	137143	none found
GABA-glutamate transaminase	NM_0006 63	137150	3' DELETION
GABA-glutamate transaminase	NM_0006 63	137150	ARG220LYS
Gamma-Aminobutyric Acid Receptor, Alpha- 1; Gabra1	X14766	137160	Dinucleotide repeat
Gamma-Aminobutyric Acid Receptor Subunit Rho1	M62400	137161	PstI
Gamma-Aminobutyric	M86868	137162	none found

Page 1262

Glutamate	X07674	138130	G/A at nt 955	
dehydrogenase 1				
Glutamate	X07674	138130	TaqI	
dehydrogenase 1				
Glutamate	X07674	138130		GLY446ASP
dehydrogenase 1				
Glutamate	X07674	138130		GLY446SER
dehydrogenase 1				
Glutamate	X07674	138130		HIS454TYR
dehydrogenase 1				
Glutamate	X07674	138130		SER445LEU
dehydrogenase 1				
Glutamate	X07674	138130		SER448PRO
dehydrogenase 1				
mitochondrial	NM_0020	138150	none found	
glutamate oxaloacetate	80			
transaminase 2/GOT2				
soluble glutamate	NM_0020	138180	none found	
oxaloacetate	79			
transaminase 1/GOT1				
Glutamate Receptor,	U16127	138243	none found	
Ionotropic, Kainate 3;				
Grik3				
Glutamate Receptor,	S75105	138244	trinucleotide repeat	
Ionotropic, Kainate 2;			3'	
Grik2				
Glutamate Receptor,	U16125	138245	none found	
Ionotropic, Kainate 1;				
Grik1				
Glutamate Receptor,	NM_0008	138246	none found	
Ionotropic, Ampa 4;	29			

Gria4	L20814	138247	none found
Glutamate Receptor, Ionotropic, Ampa 2;			
Gria2	M64752	138248	none found
Glutamate Receptor, Ionotropic, Ampa 1;			
Gria1	L13266	138249	none found
Glutamate Receptor, Ionotropic, N-Methyl- D-Asp 1; Grin1			
Glutamate Receptor, Ionotropic, N-Methyl- D-Asp A; GrinA	*****	138251	none found
Glutamate Receptor, Ionotropic, N-Methyl- D-Asp 2b; Grin2b	U28758	138252	none found
Glutamate Receptor, Ionotropic, N-Methyl- D-Asp 2a; Grin2a	U09002	138253	none found
Glutamate Receptor, Ionotropic, N-Methyl- D-Asp 2c; Grin2c	L76224	138254	none found
Glutamate decarboxylase 2 (brain, 65kD)	X69936	138275	(CA) repeat polymorphism
Glutamate decarboxylase 3		138276	none found
Glycine Receptor, Alpha-1 Subunit; Glral	X52009	138491	null allele
Glycine Receptor, Alpha-1 Subunit; Glral	X52009	138491	ARG271GLN

Glycine Receptor, Alpha-1 Subunit; Glra1	X52009	138491	ARG271LEU
Glycine Receptor, Alpha-1 Subunit; Glra1	X52009	138491	GLN266HIS
Glycine Receptor, Alpha-1 Subunit; Glra1	X52009	138491	ILE244ASN
Glycine Receptor, Alpha-1 Subunit; Glra1	X52009	138491	LYS276GLU
Glycine Receptor, Alpha-1 Subunit; Glra1	X52009	138491	P250T
Glycine Receptor, Alpha-1 Subunit; Glra1	X52009	138491	TYR279CYS
Glycine Receptor, Beta Subunit; Glrb	U33267	138492	none found
gonadotropin releasing hormone receptor/G protein- coupled/LHRHR/GNR HR	NM_0004 06	138850	ARG262GLN
gonadotropin releasing hormone receptor/G protein- coupled/LHRHR/GNR HR	NM_0004 06	138850	GLN106ARG
gonadotropin releasing hormone receptor/G protein- coupled/LHRHR/GNR HR	NM_0004 06	138850	Mae III
gonadotropin releasing hormone receptor/G	NM_0004 06	138850	TYR284CYS

protein-coupled/LHRHR/GNRHR	U34195	139191	IVS8DS, G-C, -1 alternative splice
growth hormone releasing hormone receptor/G protein-coupled/GHRHR	U34195	139191	1-BP DEL frameshift
growth hormone releasing hormone receptor/G protein-coupled/GHRHR	U34195	139191	2-BP DEL frameshift
growth hormone releasing hormone receptor/G protein-coupled/GHRHR	U34195	139191	C to T codon 236. silent
growth hormone releasing hormone receptor/G protein-coupled/GHRHR	U34195	139191	EX4,6DEL
growth hormone releasing hormone receptor/G protein-coupled/GHRHR	U34195	139191	GAA180GAG silent
growth hormone releasing hormone receptor/G protein-coupled/GHRHR	U34195	139191	IVS4DS, G-A, +1 alternative splice

growth hormone releasing hormone receptor/G protein- coupled/GHRHR	U34195	139191	IVS6AS, G-T, -1	
growth hormone releasing hormone receptor/G protein- coupled/GHRHR	U34195	139191	IVS8AS, G-C, -1	
growth hormone releasing hormone receptor/G protein- coupled/GHRHR	U34195	139191	IVS9DS, G-A, +1 frameshift	
growth hormone releasing hormone receptor/G protein- coupled/GHRHR	U34195	139191	P561T	
growth hormone releasing hormone receptor/G protein- coupled/GHRHR	U34195	139191	ARG161CYS	
growth hormone releasing hormone receptor/G protein- coupled/GHRHR	U34195	139191	ARG217TER	
growth hormone releasing hormone receptor/G protein- coupled/GHRHR	U34195	139191	ARG43TER	
growth hormone releasing hormone receptor/G protein- coupled/GHRHR	U34195	139191	ASP152HIS	

SD-114141.1

coupled/GHRHR growth hormone releasing hormone receptor/G protein- coupled/GHRHR	U34195	139191	CYS38TER
growth hormone releasing hormone receptor/G protein- coupled/GHRHR	U34195	139191	GLN154PRO
growth hormone releasing hormone receptor/G protein- coupled/GHRHR	U34195	139191	GLU224ASP
growth hormone releasing hormone receptor/G protein- coupled/GHRHR	U34195	139191	GLU224TER
growth hormone releasing hormone receptor/G protein- coupled/GHRHR	U34195	139191	GLU44LYS
growth hormone releasing hormone receptor/G protein- coupled/GHRHR	U34195	139191	ILE153THR
growth hormone releasing hormone receptor/G protein- coupled/GHRHR	U34195	139191	PHE96SER
growth hormone releasing hormone receptor/G protein- coupled/GHRHR	U34195	139191	PRO131GLN

receptor/G protein-coupled/GHRHR growth hormone releasing hormone receptor/G protein-coupled/GHRHR growth hormone releasing hormone receptor/G protein-coupled/GHRHR	U34195	139191	VAL144ILE
	U34195	139191	VAL155GLY
	M64799	142703	A649G
	M60445	142704	none found
	NM_0008	142910	HgiAI
	NM_0008	142910	ScrFI polymorphism in the 2nd intron
	NM_0004	147450	T-G, -10, 9-BP INS
	NM_0004	147450	VS4AS, A-G, -11
	NM_0004	147450	ALA145THR
	NM_0004	147450	ALA4THR
Histamine receptor H2 Histidine Decarboxylase HMGCoA reductase/HMGCR HMGCoA reductase/HMGCR Superoxide Dismutase 1/SOD1 (soluble) Superoxide Dismutase 1/SOD1 (soluble) Superoxide Dismutase 1/SOD1 (soluble) Superoxide Dismutase 1/SOD1 (soluble) Superoxide Dismutase 1/SOD1 (soluble) Superoxide Dismutase 1/SOD1 (soluble)	M64799	142703	A649G
	M60445	142704	none found
	NM_0008	142910	HgiAI
	NM_0008	142910	ScrFI polymorphism in the 2nd intron
	NM_0004	147450	T-G, -10, 9-BP INS
	NM_0004	147450	VS4AS, A-G, -11
	NM_0004	147450	ALA145THR
	NM_0004	147450	ALA4THR
	NM_0004	147450	ALA4VAL
	NM_0004	147450	ASP90ALA
Superoxide Dismutase 1/SOD1 (soluble) Superoxide Dismutase 1/SOD1 (soluble) Superoxide Dismutase 1/SOD1 (soluble) Superoxide Dismutase 1/SOD1 (soluble) Superoxide Dismutase 1/SOD1 (soluble) Superoxide Dismutase 1/SOD1 (soluble)	NM_0004	147450	CYS6PHE

Superoxide Dismutase 1/SOD1 (soluble)	NM_0004 54	147450	GLU100GLY
Superoxide Dismutase 1/SOD1 (soluble)	NM_0004 54	147450	GLU21LYS
Superoxide Dismutase 1/SOD1 (soluble)	NM_0004 54	147450	GLY16SER
Superoxide Dismutase 1/SOD1 (soluble)	NM_0004 54	147450	GLY37ARG
Superoxide Dismutase 1/SOD1 (soluble)	NM_0004 54	147450	GLY41ASP
Superoxide Dismutase 1/SOD1 (soluble)	NM_0004 54	147450	GLY41SER
Superoxide Dismutase 1/SOD1 (soluble)	NM_0004 54	147450	GLY72SER
Superoxide Dismutase 1/SOD1 (soluble)	NM_0004 54	147450	GLY85ARG
Superoxide Dismutase 1/SOD1 (soluble)	NM_0004 54	147450	GLY93ALA
Superoxide Dismutase 1/SOD1 (soluble)	NM_0004 54	147450	GLY93CYS
Superoxide Dismutase 1/SOD1 (soluble)	NM_0004 54	147450	HIS43ARG
Superoxide Dismutase 1/SOD1 (soluble)	NM_0004 54	147450	HIS46ARG
Superoxide Dismutase 1/SOD1 (soluble)	NM_0004 54	147450	ILE104THE
Superoxide Dismutase 1/SOD1 (soluble)	NM_0004 54	147450	ILE113THR
Superoxide Dismutase 1/SOD1 (soluble)	NM_0004 54	147450	LEU106VAL
Superoxide Dismutase 1/SOD1 (soluble)	NM_0004 54	147450	LEU126TER

1/SOD1 (soluble)	54				LEU144SER
Superoxide Dismutase	NM_0004	147450			
1/SOD1 (soluble)	54				LEU38VAL
Superoxide Dismutase	NM_0004	147450			
1/SOD1 (soluble)	54				LEU84VAL
Superoxide Dismutase	NM_0004	147450			
1/SOD1 (soluble)	54				SER134ASN
Superoxide Dismutase	NM_0004	147450			
1/SOD1 (soluble)	54				THR151ILE
Superoxide Dismutase	NM_0004	147450			Val7-->Glu
1/SOD1 (soluble)	54				
Superoxide dismutase	X02317	147450			
1 (Cu/Zn)					
Superoxide Dismutase	X65965	147460			ALA16VAL
2/SOD2					
(mitochondrial)					
Human clone pSK1	U05875	147569			Gln64Arg
interferon gamma					
receptor accessory					
factor-1 (AF-1)					
mRNA, complete cds					
MICROTUBULE-	J03778	157140			+39deltaG iron 4
ASSOCIATED					
PROTEIN TAU					
MICROTUBULE-	J03778	157140			IVS10, A-G, +13
ASSOCIATED					
PROTEIN TAU					
MICROTUBULE-	J03778	157140			IVS10, C-U, +14
ASSOCIATED					

PROTEIN TAU	J03778	157140	IVS10, C-U, +16	
MICROTUBULE-ASSOCIATED				
PROTEIN TAU	J03778	157140	IVS10, G-A, +1	
MICROTUBULE-ASSOCIATED				
PROTEIN TAU	J03778	157140		ARG406TRP
MICROTUBULE-ASSOCIATED				
PROTEIN TAU	J03778	157140		ASN279LYS
MICROTUBULE-ASSOCIATED				
PROTEIN TAU	J03778	157140		GLY272VAL
MICROTUBULE-ASSOCIATED				
PROTEIN TAU	J03778	157140		PRO301LEU
MICROTUBULE-ASSOCIATED				
PROTEIN TAU	J03778	157140		SER305ASN
MICROTUBULE-ASSOCIATED				
PROTEIN TAU	J03778	157140		VAL337MET
MICROTUBULE-ASSOCIATED				
nerve growth factor receptor/NGFR	NM_002507	162010		HincII
nerve growth factor receptor/NGFR	NM_002507	162010		HindIII
nerve growth factor receptor/NGFR	NM_002507	162010	Two TaqI sites	

nerve growth factor receptor/NGFR	NM_0025 07	162010	XmnI	
H.sapiens encoding PC1/PC3	X64810	162150	IVS5DS, A-C, +4	
H.sapiens encoding PC1/PC3	X64810	162150		GLY483ARG
Tachykinin NK2 receptor/TACR2	M57414	162321	none found	
Tachykinin NK1 receptor/TACR1	M81797	162323	none found	
Tachykinin NK3 receptor/TACR3	M89473	162332	none found	
neuromedin B receptor/g protein- coupled/NMBR	*****	162341	none found	
Neuropeptide Y	K01911	162640		LEU7PRO
Neuropeptide Y receptor Y1/NPY1R	M84755	162641	none found	
Neuropeptide Y receptor Y2/NPY2R	U32500	162642	none found	
Neuropeptide Y receptor Y3/chemokine receptor 4/CXCR4	X71635	162643	none found	
Neurotensin receptor	X70070	162651	Tetranucleotide repeat	
Human AD amyloid mRNA, complete cds	L08850	163890	Dinucleotide repeat	
Human AD amyloid mRNA, complete cds	L08850	163890		ALA30PRO
Human AD amyloid mRNA, complete cds	L08850	163890		ALA53THR

Human AD amyloid mRNA, complete cds	L08850	163890	G209A
Solute carrier family 6, member 43	NM_0010	163970	none found
5/SLC6A2/NAT1/NET 1 (glycine)			
Human obese (ob)	U18915	164160	-1387 G/A
mRNA, complete cds			
Human obese (ob)	U18915	164160	1-BP DEL frameshift
mRNA, complete cds			
Human obese (ob)	U18915	164160	A --> G + 19 exon1
mRNA, complete cds			
Human obese (ob)	U18915	164160	C(-188)A
mRNA, complete cds			
Human obese (ob)	U18915	164160	ARG105TRP
mRNA, complete cds			
Human obese (ob)	U18915	164160	Glu-126-Gln
mRNA, complete cds			
Human obese (ob)	U18915	164160	Ser-91-Ser
mRNA, complete cds			
Opioid Receptor, Delta-1; Oprd1	U10504	165195	T to C in codon 307 silent
Opioid Receptor, Kappa-1; Oprk1	U17298	165196	none found
Oxytocin receptor	X64878	167055	C to T exon 3
Oxytocin receptor	X64878	167055	CA repeat
Human peptidylglycine alpha-amidating monooxygenase	M37721	170270	none found
mRNA, complete cds			
Phenol-preferring	NM_0010	171150	Arg213His

SD-111111.1

sulfotransferase, family 1A, member 1/SLIT1A1	55			
phenylethanolamine N-methyltransferase/PNMT	NM_002686	171190	BANI	
phospholipid transfer protein/PLTP	NM_006227	172425	TaqIB	
Methenyltetrahydrofolate cyclohydrolase	J04031	172460	ARG293HIS	
prolactin receptor/PRLR	NM_000949	176761	none found	
Adrenocorticotrophic hormone (ACTH)	M28636	176830	3804C-A	
Adrenocorticotrophic hormone (ACTH)	M28636	176830	7013G-T	
Adrenocorticotrophic hormone (ACTH)	M28636	176830	7133C DEL	
butyrylcholinesterase 1/serum cholinesterase 1/BCHE1	NM_000055	177400	209 A/G Asp-70 to Gly	
butyrylcholinesterase 1/serum cholinesterase 1/BCHE1	NM_000055	177400	342-bp Alu in exon two	
butyrylcholinesterase 1/serum cholinesterase 1/BCHE1	NM_000055	177400	A-to-G Y128C	
butyrylcholinesterase 1/serum cholinesterase 1/BCHE1	NM_000055	177400	GCA to ACA ALA539THR	
butyrylcholinesterase 1/BCHE1	NM_000055	177400	GGT to GTT Gly 390 to Val	

1/serum cholinesterase	55			
1/B ₅ HEI				
butyrylcholinesterase	NM_0000	177400	GGT-to-GGAG Gly 117	
1/serum cholinesterase	55		Frameshift	
1/B ₅ HEI				
butyrylcholinesterase	NM_0000	177400	E451X	
1/serum cholinesterase	55			
1/B ₅ HEI				
butyrylcholinesterase	NM_0000	177400	F446V	
1/serum cholinesterase	55			
1/B ₅ HEI				
butyrylcholinesterase	NM_0000	177400	G365R	
1/serum cholinesterase	55			
1/B ₅ HEI				
butyrylcholinesterase	NM_0000	177400	GLU497VAL	
1/serum cholinesterase	55			
1/B ₅ HEI				
butyrylcholinesterase	NM_0000	177400	Gly115 by Asp	
1/serum cholinesterase	55			
1/B ₅ HEI				
butyrylcholinesterase	NM_0000	177400	LEU330ILE	
1/serum cholinesterase	55			
1/B ₅ HEI				
butyrylcholinesterase	NM_0000	177400	Q119X	
1/serum cholinesterase	55			
1/B ₅ HEI				
butyrylcholinesterase	NM_0000	177400	R515C	
1/serum cholinesterase	55			
1/B ₅ HEI				
butyrylcholinesterase	NM_0000	177400	THR243MET	
1/serum cholinesterase	55			

1/B ₀ HE1				THR250PRO
butyrylcholinesterase	NM_0000	177400		
1/serum cholinesterase	55			
1/B ₀ HE1				
butyrylcholinesterase	NM_0000	177400		
1/serum cholinesterase	55			
1/B ₀ HE1				
butyrylcholinesterase	*****	177500	none found	
2/serum cholinesterase				
2/B ₀ HE2				
retinoic acid receptor	M57707	180190	none found	
gamma/RARG				
retinoic acid receptor	NM_0009	180220	none found	
beta RARB	65			
retinoic acid receptor	NM_0009	180240	7-base deletion frameshift	
alpha/RARA	64			
retinoic acid receptor	NM_0009	180240	codon 411 C to T	
alpha/RARA	64			Arg272Gln
retinoic acid receptor	NM_0009	180240		Met297Leu
alpha/RARA	64			
retinoic acid receptor	NM_0009	180245	none found	
retinoid X receptor	57			
alpha/RXRA				
retinoid X receptor	X66424	180246	none found	
beta RXRB				
retinoid X receptor	U38480	180247	none found	
gamma/RXRG				
serotonin 5-HT	M81590	182131	C129T	
receptors 5-HT1B, G				
protein-coupled				

serotonin 5-HT receptors 5-HT1B, G protein-coupled	M81590	182131	G861C	
serotonin 5-HT receptors 5-HT1E, G protein-coupled	M91467	182132	none found	
serotonin 5-HT receptors 5-HT1D, G protein-coupled	M81590	182133	silent polymorphism	
serotonin 5-HT receptors 5-HT1F, G protein-coupled	L05597	182134	none found	
serotonin 5-HT receptors 5-HT2A, G protein-coupled	D87030	182135	-1438G/A.	
serotonin 5-HT receptors 5-HT2A, G protein-coupled	D87030	182135	102T-C	
serotonin 5-HT receptors 5-HT2A, G protein-coupled	D87030	182135	HpaII	
serotonin 5-HT receptors 5-HT2A, G protein-coupled	D87030	182135	His452Tyr	
serotonin 5-HT receptors 5-HT7, G protein-coupled	L21195	182137	none found	
serotonin transporter	X70697	182138	PstI	
serotonin transporter	X70697	182138	promoter 44-bp ins/del	
serotonin transporter	X70697	182138	tandem repeat close	

SD - H1411

serotonin transporter	X70697	182138	to the promoter two polyadenylation sites
serotonin transporter	X70697	182138	VNTR intron 2
serotonin transporter	X70697	182138	silent polymorphism
serotonin 5-HT receptors 5-HT3, gated ion channel	D49394	182139	none found
type I voltage dependent sodium channel alpha subunit/SCN1A	S71446	182389	none found
type II voltage dependent sodium channel alpha 1 subunit/SCN2A1	M94055	182390	none found
type III voltage dependent sodium channel alpha subunit/SCN3A	S69887	182391	none found
type VI voltage dependent sodium channel alpha subunit/SCN6A	M55662	182392	none found
Somatostatin receptor 1/G protein-coupled	M81829	182451	(CA) _n 5'
Somatostatin receptor 2	M81830	182452	TRP188TER
Somatostatin receptor 3/adrenyl cyclase coupled	M96738	182453	none found

SD-11141.1

Somatostatin receptor 4	L07833	182454	none found	
Somatostatin receptor 5	D16827	182455	2 RFLP's promoter	
human rapamycin-binding protein (FKBP-1) mRNA, complete cds	M65128	186946	none found	
thyrotropin releasing hormone receptor/G protein coupled/TRHR	X75071	188545	9-BP DEL deletion of 3 amino acids	
thyrotropin releasing hormone receptor/G protein coupled/TRHR	X75071	188545		ALA118THR
thyrotropin releasing hormone receptor/G protein coupled/TRHR	X75071	188545		ARG171TER
oncogene NM_001982	NM_001982	190151	none found	
ERBB3/HER3	X52836	191060	-5806G>T	
tryptophan Hydroxylase; TPH	X52836	191060	-6526A>G	
tryptophan Hydroxylase; TPH	X52836	191060	-7065C>T	
tryptophan Hydroxylase; TPH	X52836	191060	7180T>G	
tryptophan Hydroxylase; TPH	X52836	191060	A218C in intron 7	
tryptophan Hydroxylase; TPH	X52836	191060	A779C	
tryptophan Hydroxylase; TPH	X52836	191060	A779C in intron 7	

SD-11114.1

tryptophan	X52836	191060	T1095C
Hydroxylase; tPH			
Human tryptophan	U32989	191070	6G->T intron
oxygenase (TDO)			
mRNA, complete cds			
Human tryptophan	U32989	191070	CCCCCT repeat
oxygenase (TDO)			
mRNA, complete cds			
Human tryptophan	U32989	191070	GTT repeat
oxygenase (TDO)			
mRNA, complete cds			
tyrosine Hydroxylase	X05290	191290	(TCAT)n intron 1
tyrosine Hydroxylase	X05290	191290	BglII
tyrosine Hydroxylase	X05290	191290	DraI
tyrosine Hydroxylase	X05290	191290	PstI
tyrosine Hydroxylase	X05290	191290	ScaI
tyrosine Hydroxylase	X05290	191290	T-229A
tyrosine Hydroxylase	X05290	191290	[AATG]n
tyrosine Hydroxylase	X05290	191290	ARG233HIS
tyrosine Hydroxylase	X05290	191290	GLN381LYS
tyrosine Hydroxylase	X05290	191290	LEU205PRO
tyrosine Hydroxylase	X05290	191290	Val468Met
tyrosine Hydroxylase	X05290	191290	Val81Met
neurotrophic tyrosine	Y09033	191315	1-BP DEL, 1726C frameshift
kinase receptor type			
1/NTRK1			
neurotrophic tyrosine	Y09033	191315	1810C>T
kinase receptor type			
1/NTRK1			
neurotrophic tyrosine	Y09033	191315	1838G>T
kinase receptor type			

1/NTRK1 neurotrophic tyrosine kinase receptor type 1/NTRK1	Y09033	191315	G1795C GLY571ARG
neurotrophic tyrosine kinase receptor type 1/NTRK1	Y09033	191315	IVS4, G-C, -1
neurotrophic tyrosine kinase receptor type 1/NTRK1	Y09033	191315	IVSDS, A-C, +3
neurotrophic tyrosine kinase receptor type 1/NTRK1	Y09033	191315	ARG774PRO
neurotrophic tyrosine kinase receptor type 1/NTRK1	Y09033	191315	ARG85SER]
neurotrophic tyrosine kinase receptor type 1/NTRK1	Y09033	191315	GLN9TER
neurotrophic tyrosine kinase receptor type 1/NTRK1	Y09033	191315	GLY607VAL
neurotrophic tyrosine kinase receptor type 1/NTRK1	Y09033	191315	HIS598TYR
neurotrophic tyrosine kinase receptor type 1/NTRK1	NM_0025 30	191316	none found
vasoactive intestinal peptide receptor 1/VIPR1	***** 3/NTRK3	192321	none found

SD-14141.1

Vesicular Amine Transporter 2; VAT2	L09118	193001	TaqI	
Vesicular Amine Transporter 1; VAT1	*****	193002	none found	
melanocortin 2 receptor/ACTH	NM_0005 29	202200	1-BP INS frameshift	
receptor/MC2R melanocortin 2 receptor/ACTH	NM_0005 29	202200	ARG128CYS	
receptor/MC2R melanocortin 2 receptor/ACTH	NM_0005 29	202200	ARG201TER	
receptor/MC2R melanocortin 2 receptor/ACTH	NM_0005 29	202200	ASP107ASN	
receptor/MC2R melanocortin 2 receptor/ACTH	NM_0005 29	202200	CYS251PHE	
receptor/MC2R melanocortin 2 receptor/ACTH	NM_0005 29	202200	SER120ARG	
receptor/MC2R melanocortin 2 receptor/ACTH	NM_0005 29	202200	SER74ILE	
dopamine beta hydroxylase	Y00096	223360		
glutamate formiminotransferase/d	*****	229100	none found	
ihydrofolate synthetase 5,10-	U09806	236250	1027T-G	

SD-141141.1

@METHYLENETET RAHYDROFOLATE REDUCTASE 5,10-	U09806	236250	1084C-T
@METHYLENETET RAHYDROFOLATE REDUCTASE 5,10-	U09806	236250	1298A-C
@METHYLENETET RAHYDROFOLATE REDUCTASE 5,10-	U09806	236250	1711C-T
@METHYLENETET RAHYDROFOLATE REDUCTASE 5,10-	U09806	236250	677C-T ala --> val
@METHYLENETET RAHYDROFOLATE REDUCTASE 5,10-	U09806	236250	983A-G
@METHYLENETET RAHYDROFOLATE REDUCTASE 5,10-	U09806	236250	exon 7 Ala-->Glu
@METHYLENETET RAHYDROFOLATE REDUCTASE 5,10-	U09806	236250	A225V

SD-114141.1

5,10- @METHYLENETET RAHYDROFOLATE REDUCTASE	U09806	236250	ARG158GLN
5,10- @METHYLENETET RAHYDROFOLATE REDUCTASE	U09806	236250	ARG184TER
Glycine cleavage system: Protein T	D13811	238310	1-BP DEL, 183C
Glycine cleavage system: Protein T	D13811	238310	ASP276HIS
Glycine cleavage system: Protein T	D13811	238310	GLY269ASP
Glycine cleavage system: Protein T	D13811	238310	GLY47ARG
Glycine cleavage system: Protein T	D13811	238310	HIS42ARG
6-pyruvoyl tetrahydrobiopterin synthase/PTPS	Q03393	261640	14-BP DEL K120-->Stop
6-pyruvoyl tetrahydrobiopterin synthase/PTPS	Q03393	261640	ARG16CYS
6-pyruvoyl tetrahydrobiopterin synthase/PTPS	Q03393	261640	ARG25GLN
6-pyruvoyl tetrahydrobiopterin synthase/PTPS	Q03393	261640	ASN47ASP
6-pyruvoyl tetrahydrobiopterin synthase/PTPS	Q03393	261640	ASN52SER

SD-111111.1

tetrahydrobiopterin synthase/PTPS 6-pyruvoyl	Q03393	261640	ASP116GLY
tetrahydrobiopterin synthase/PTPS 6-pyruvoyl	Q03393	261640	ASP96ASN
tetrahydrobiopterin synthase/PTPS 6-pyruvoyl	Q03393	261640	D136V
tetrahydrobiopterin synthase/PTPS 6-pyruvoyl	Q03393	261640	K129E
tetrahydrobiopterin synthase/PTPS 6-pyruvoyl	Q03393	261640	PRO87SER
tetrahydrobiopterin synthase/PTPS 6-pyruvoyl	Q03393	261640	T67M
tetrahydrobiopterin synthase/PTPS 6-pyruvoyl	Q03393	261640	VAL56MET
Glutamate decarboxylase 1 (brain, 67kD)	M81883	266100	none found
Human hydroxyindole- O-methyltransferase promoter A-derived (HIOMT) mRNA, complete cds	U11090	300015	none found

angiotensin II receptor type 2/AGTR2	U10273	300034	none found
P2Y4 pyrimidinergic receptor/Gi protein- coupled	NM_0025 65	300038	none found
Gamma-Aminobutyric Acid Receptor, Epsilon; Gabre	Y09765	300093	none found
bombesin-like receptor 3/BRS3	NM_0017 27	300107	none found
Glutamate dehydrogenase 2	U08997	300144	none found
ACETYLCHOLINERGIC N METHYLTRANSFERASE-LIKE	300162		none found
Arginine vasopressin receptor 2	AF030626	304800	1-BP DEL
Arginine vasopressin receptor 2	AF030626	304800	1-BP DEL, 102G
Arginine vasopressin receptor 2	AF030626	304800	1-BP INS frameshift
Arginine vasopressin receptor 2	AF030626	304800	1-BP INS 804 frameshift
Arginine vasopressin receptor 2	AF030626	304800	15delC
Arginine vasopressin receptor 2	AF030626	304800	28-bp del
Arginine vasopressin receptor 2	AF030626	304800	786delG frameshift
Arginine vasopressin	AF030626	304800	CpG dinucleotides

receptor 2	ALA132ASP			
Arginine vasopressin receptor 2	ARG181CYS			
Arginine vasopressin receptor 2	ARG113TRP			
Arginine vasopressin receptor 2	ARG203CYS			
Arginine vasopressin receptor 2	ARG337TER			
Arginine vasopressin receptor 2	ASP85ASN			
Arginine vasopressin receptor 2	G107E			
Arginine vasopressin receptor 2	GLY185CYS			
Arginine vasopressin receptor 2	GLY201ASP			
Arginine vasopressin receptor 2	L43P			
Arginine vasopressin receptor 2	P322H			
Arginine vasopressin receptor 2	P322S			
Arginine vasopressin receptor 2	R137H			
Arginine vasopressin receptor 2	TRP71TER			
Arginine vasopressin receptor 2	TYR205CYS			

Arginine vasopressin receptor 2	AF030626	304800	TYR280CYS
Arginine vasopressin receptor 2	AF030626	304800	W193X
Gamma-Aminobutyric Acid Receptor, Alpha-3; Gabra3	S62908	305660	16-repeat allele
Gamma-Aminobutyric Acid Receptor, Alpha-3; Gabra3	S62908	305660	Dinucleotide repeat
gastrin-releasing polypeptide receptor/G protein-coupled/GRPR	D87058	305670	two single nucleotide substitutions in exon 2
Glutamate Receptor, Ionotropic, Ampa 3; Glra3	X82068	305915	none found
Glycine Receptor, Alpha-2 Subunit; Glra2	X52008	305990	none found
Monoamine Oxidase A; MAOA	M69226	309850	23-bp VNTR
Monoamine Oxidase A; MAOA	M69226	309850	3rd base of codon 941 941 G>T
Monoamine Oxidase A; MAOA	M69226	309850	A1026T ProlineProline
Monoamine Oxidase A; MAOA	M69226	309850	A1559G LysineArginine
Monoamine Oxidase A; MAOA	M69226	309850	A385C ArginineArginine _e
Monoamine Oxidase A; MAOA	M69226	309850	C1410T Aspartic AcidAspartic

Monoamine Oxidase A; MAOA	M69226	309850	Acid C886T Glutamine296T ermination codon
Monoamine Oxidase A; MAOA	M69226	309850	C886T GlutamineTermin ation codon
Monoamine Oxidase A; MAOA	M69226	309850	exon 14 -- RFLP (EcoRV enzyme)
Monoamine Oxidase A; MAOA	M69226	309850	length of (CA) _n repeat
Monoamine Oxidase A; MAOA	M69226	309850	RFLP (EcoRV enzyme)
Monoamine Oxidase A; MAOA	M69226	309850	RFLP (Pst I)
Monoamine Oxidase A; MAOA	M69226	309850	T891G ArginineArginin e
Monoamine Oxidase A; MAOA	M69226	309850	T891G
Monoamine Oxidase B; MAOB	M69177	309860	(GT) _n repeat
Monoamine Oxidase B; MAOB	M69177	309860	36 bases upstream from intron 13-exon 14 boundary
Monoamine Oxidase B; MAOB	M69177	309860	A at position 644 of intron 13
Monoamine Oxidase B; MAOB	M69177	309860	G at position 644 of intron 13
Monoamine Oxidase B; MAOB	M69177	309860	RFLP (MaeIII enzyme)
serotonin 5-HT receptors 5-HT1C, G	U49516	312861	2831T > G in the 3'

SD-144141.1

protein-coupled serotonin 5-HT receptors 5-HT1C, G	U49516	312861	CYS23SER
protein-coupled			
androgen receptor	M20132	313700	Hind III
androgen receptor	M20132	313700	(CAA)n
androgen receptor	M20132	313700	(CAG)n
androgen receptor	M20132	313700	(GGN)n
androgen receptor	M20132	313700	5-KB DEL, EX F, G
androgen receptor	M20132	313700	5-KB DEL, EX E
androgen receptor	M20132	313700	C>T within exon B silent
androgen receptor	M20132	313700	CAG340TAG Gln>Ter
androgen receptor	M20132	313700	Del T at 3286 frameshift
androgen receptor	M20132	313700	dell893 frameshift
androgen receptor	M20132	313700	G Codon 210 A
androgen receptor	M20132	313700	G Codon 211 A
androgen receptor	M20132	313700	G2314A ala>thr
androgen receptor	M20132	313700	G2677A glu629arg
androgen receptor	M20132	313700	HhaI
androgen receptor	M20132	313700	HpaII
androgen receptor	M20132	313700	Insert of 69
			nucleotides
			MaeIII
			PARTIAL DEL
			Stu I
			598 or 599 ter
			ALA721THR
			ALA771THR
			ARG607GLN
			ARG608LYS
			Arg615His

androgen receptor	M20132	313700	arg726leu
androgen receptor	M20132	313700	Arg752Gln
androgen receptor	M20132	313700	ARG772CYS
androgen receptor	M20132	313700	ARG773CYS
androgen receptor	M20132	313700	ARG773HIS
androgen receptor	M20132	313700	ARG839CYS
androgen receptor	M20132	313700	ARG839HIS
androgen receptor	M20132	313700	arg840his
androgen receptor	M20132	313700	ARG846HIS
androgen receptor	M20132	313700	ARG855HIS
androgen receptor	M20132	313700	CYS579PHE
androgen receptor	M20132	313700	G214R
androgen receptor	M20132	313700	GLN60TER
androgen receptor	M20132	313700	Gln798Glu
androgen receptor	M20132	313700	GLN902ARG
androgen receptor	M20132	313700	GLU2LYS
androgen receptor	M20132	313700	gly743val
androgen receptor	M20132	313700	HIS874TYR
androgen receptor	M20132	313700	ILE869MET
androgen receptor	M20132	313700	LEU172TER
androgen receptor	M20132	313700	LEU676PRO
androgen receptor	M20132	313700	LEU707ARG
androgen receptor	M20132	313700	LYS588TER
androgen receptor	M20132	313700	LYS882TER
androgen receptor	M20132	313700	MET780ILE
androgen receptor	M20132	313700	MET786VAL
androgen receptor	M20132	313700	PHE582TYR
androgen receptor	M20132	313700	PRO546SER
androgen receptor	M20132	313700	pro892ser
androgen receptor	M20132	313700	SER647ASN
androgen receptor	M20132	313700	THR877ALA

androgen receptor	M20132	313700	THR877SER
androgen receptor	M20132	313700	TRP717TER
androgen receptor	M20132	313700	TRP794TER
androgen receptor	M20132	313700	TYR761CYS
androgen receptor	M20132	313700	val 581 phe
androgen receptor	M20132	313700	VAL730MET
androgen receptor	M20132	313700	VAL865LEU
androgen receptor	M20132	313700	VAL865MET
androgen receptor	M20132	313700	VAL866MET
ACETYL-SEROTONI		402500	none found

METHYLTRANSFERASE, Y-N

CHROMOSOMAL

voltage dependent	U07139	600003	none found
calcium channel beta 2			
subunit 2 ACNB2			
vascular angiotensin II	NM_0048	600015	none found
receptor type	35		
1B/AGTR1B			
Opioid Receptor, Mu-	NM_0009	600018	(CA)n
1; Oprm1	14		
Opioid Receptor, Mu-	NM_0009	600018	Asn40Asp
1; Oprm1	14		
P2Y2 purinoceptor/G	U07225	600041	none found
protein-coupled			
Solute Carrier Family	U03504	600111	none found
1, Member 3; Slc1a3			
type V voltage	NM_0003	600163	1-BP DEL frameshift
dependent sodium	35		
channel alpha			

Page 1294

Acid Receptor, Beta-2; Gabbr2	NM_0008 16	600233	none found	
Gamma-Aminobutyric Acid Receptor, Gamma-3; Gabbr3	NM_0010 37	600235		CYS121TRP
type I voltage dependent sodium channel beta subunit/SCN1B				
Arginine Vasopressin Receptor 1B/AVPR1B	AF030512	600264	none found	
Glutamate Receptor, Ionotropic, Kainate 4; Grik4	S67803	600282	none found	
Glutamate Receptor, Ionotropic, Kainate 5; Grik5	S40369	600283	none found	
Solute Carrier Family 1, Member 2; Slc1a2	U03505	600300	none found	
Vesicular acetylcholine transporter	NM_0030 55	600336	none found	
bradykinin receptor B1/BDKRB1 G	NM_0007 10	600337	9-base pair deletion	
protein-coupled bradykinin receptor B1/BDKRB1 G	NM_0007 10	600337	A1098-->G	
protein-coupled bradykinin receptor B1/BDKRB1 G	NM_0007 10	600337	C181-->T	

SD:111111

Page 1295

bradykinin receptor B1/BDKRB1 G protein-coupled	NM_0007 10	600337	G-699-->C
Glycine Receptor, Alpha-3 Subunit; Glra3	AF018157	600421	none found
Adenosine A3 Receptor; Adora3/G protein-coupled	L20463	600445	none found
Adenosine A2b Receptor; Adora2b/G protein-coupled	X68487	600446	none found
neurotrophic tyrosine kinase receptor type 2/NTRK2	NM_0061 80	600456	none found
inwardly rectifying potassium channel, subfamily J, member 4/KCNJ4	NM_0049 81	600504	none found
reelin/RELN	NM_0050 45	600514	none found
Human immunophilin (FKBP52) mRNA, complete cds	M88279	600611	none found
opioid binding cell adhesion molecule OBCAM	*****	600632	none found
Solute carrier family 1, member 6 (GABA/GLU)/SLC1A 6	NM_0050 71	600637	none found
Human aryl	L19956	600641	none found

SD-141111

Page 1296

SD-1111

Gene	Accession	Protein	RefSeq ID	NCBI Gene ID
P2X ₃ , Ligand-Gated Ion Channel, 3; P2rx3	NM_002558	600845	none found	
Purinergic Receptor P2X ₃ , Ligand-Gated Ion Channel, 1; P2rx1	AF000234	600846	none found	
Purinergic Receptor P2X ₃ , Ligand-Gated Ion Channel, 4; P2rx4	*****	600932	none found	
G protein coupled potassium channel inward rectifier/GIRK3	600934	600934	none found	
isolate hydrolase 1/FOH1	NM_000163	600946		
growth hormone receptor/GHR	U40347	600950	none found	
serotonin N-Acetyltransferase; SNAT	NM_002303	601007	(CTTTA) _n	
leptin receptor/LEPR	NM_002303	601007	3'-UTR insertion/deletion CA microsatellite repeat in intron 3, IVS16, G-A, +1	
Ala976Asp	NM_002303	601007		
Gln223Arg	NM_002303	601007		
GLN23ARG	NM_002303	601007		

leptin receptor/LEPR	03 NM_0023	601007	K109R
leptin receptor/LEPR	03 NM_0023	601007	K656N
leptin receptor/LEPR	03 NM_0023	601007	Lys109Arg
leptin receptor/LEPR	03 NM_0023	601007	Lys656Asn
leptin receptor/LEPR	03 NM_0023	601007	Pro1019Pro
leptin receptor/LEPR	03 NM_0023	601007	Ser343Ser
leptin receptor/LEPR	03 NM_0023	601007	Ser492Thr
Solute carrier family 6, Member 9; SLC6A9 (glycine)	S70612	601019	none found
serotonin 5-HT receptors 5-HT6, G protein-coupled	L41147	601109	C267T
Glutamate Receptor, Metabotropic 3/G protein-coupled/Grm3	X77748	601115	none found
Glutamate Receptor, Metabotropic 8/G protein-coupled/Grm8	U95025	601116	none found
Thimet oligopeptidase	Z50115	601117	none found
serotonin 5-HT receptors 5-HT2B, G protein-coupled	X77307	601122	none found

P2Y ₁ purinoceptor/G protein-coupled	U42029	601167	none found
type II voltage dependent sodium channel alpha 2 subunit/SCN2A2	M55662	601219	none found
11.sapiens mRNA for aryl sulfotransferase (ST1A2)	X78282	601292	none found
serotonin 5-HT receptor 5-HT5a, G protein-coupled	X81411	601305	none found
type II voltage dependent sodium channel beta subunit/SCN2B	NM_0045 88	601327	none found
11.sapiens mRNA for prepronociceptin	X97370	601459	none found
P2Y ₇ purinoceptor/leukotrien e B4 receptor/G protein-coupled	NM_0007 52	601531	none found
G protein coupled potassium channel, subfamily J, member 3/KCNJ6GIRK1	NM_0022 39	601534	(CA)n
estrogen receptor 2 (ESR2)	X99101	601663	none found
voltage dependent potassium channel, subfamily K, member	NM_0022 45	601745	none found

1/KUNLI	NM_0003	601769	A(T/C)G	putative translation start site
vitamin D	76			
rec.ptor VDR				
vitamin D	NM_0003	601769	Apal	
rec.ptor VDR	76			
vitamin D	NM_0003	601769	BsmI	
rec.ptor VDR	76			
vitamin D	NM_0003	601769	FokI	
rec.ptor VDR	76			
vitamin D	NM_0003	601769	PvuII	
rec.ptor VDR	76			
vitamin D	NM_0003	601769	TaqI	
rec.ptor VDR	76			
vitamin D	NM_0003	601769	XbaI	
rec.ptor VDR	76			
vitamin D	NM_0003	601769		ARG-GLY
rec.ptor VDR	76			
vitamin D	NM_0003	601769		ARG391CYS
rec.ptor VDR	76			
vitamin D	NM_0003	601769		HIS305GLN
rec.ptor VDR	76			
vitamin D	NM_0003	601769		ILE314SER
rec.ptor VDR	76			
vitamin D	NM_0003	601769		ARG271LEU
rec.ptor VDR	76			
vitamin D	NM_0003	601769		ARG30TER
rec.ptor VDR	76			
vitamin D	NM_0003	601769		ARG47GLN
rec.ptor VDR	76			
vitamin D	NM_0003	601769		ARG77GLN

SD- 141-111

rec. ptor VDR	76	601769	codon 352
vitamin D	NM_000376		
rec. ptor VDR	76	601769	GLN149TER
vitamin D	NM_000376		
rec. ptor VDR	76	601769	GLY30ASP
vitamin D	NM_000376		
rec. ptor VDR	76	601769	GLY46ASP
vitamin D	NM_000376		
rec. ptor VDR	76	601769	TYR292TER
vitamin D	NM_000376		
rec. ptor VDR	76	601770	none found
Neurop. ptide Y	D86519		
rec. ptor Y6	76	601784	none found
voltage independent	NM_001094		
neu. ptide sodium	94		
channel I/AACCN1		601949	none found
voltage dependent	*****		
calcium channel beta 4		601958	none found
sub-unit CACNB4			
voltage dependent			
calcium channel beta 3	NM_000725	601970	none found
sub-unit CACNB3			
vasoactive intestinal	L40764		
peptide receptor			
2A type			
RAA related orphan	*****	601972	none found
rec. ptor B/RORB			
Opioid Receptor,	U75283	601978	Gln2Pro
Signa I			
Opioid Receptor,	U75283	601978	GC-241-240TT in the 5'
Signa I			

Neuropeptide Y receptor Y5	U94320	602001	none found
Catecholaminergic receptor 2	NM_001883	602034	none found
neuropilin 1/VEGF 165 receptor NRP1	NM_003873	602069	none found
neuropilin 2/VEGF 165 receptor NP2	NM_003872	602070	none found
Solute carrier family 29 (nucleosides), member 2/SCL29A2/ENT2	X86681	602110	none found
serotonin 5-HT receptor 5-HT4, G protein-coupled	Y08756	602164	none found
Solute carrier family 29 (nucleosides), member 1/SCL29A1/ENT1	NM_004955	602193	none found
inwardly-rectifying potassium channel, subfamily J, member 10/KCNJ10	*****	602208	none found
voltage-dependent potassium channel, KCa3.1-like subfamily, member 3/KCNQ3	AF033347	602232	GLY263VAL
voltage-dependent potassium channel, KCa3.1-like subfamily, member 2/KCNQ2	NM_000218	602235	1-BP DEL, 1846T frameshift
voltage-dependent potassium channel, member 2/KCNQ2	NM_000218	602235	5-BP INS frameshift

SD 14/01/01

	NM_000218	602235	ALA306THR
KC F-like subfamily, member 2/KCNQ2 voltage dependent potassium channel,			
KC F-like subfamily, member 2/KCNQ2 voltage dependent potassium channel,			
KC F-like subfamily, member 2/KCNQ2 voltage dependent potassium channel,			
KC F-like subfamily, member 2/KCNQ2 voltage dependent potassium channel,			
Anionic oxidase (cooper-containing) 2/AOC2	D88213	602268	none found
Gluamate Receptor, Ionotropic, Delta 2; GRII2	AF009014	602368	none found
P2 Y6 pyrimidinergic receptor G protein-coupled	NM_004154	602451	none found
opioid receptor-like 1/GPR11	X77130	602548	none found
Purinergic Receptor P2X Ligand-Gated Ion Channel 7; P2rx7	Y09561	602566	none found
Human FK506-binding protein FKBP51 mRNA, complete cds	U71321	602623	none found
P2 Y11 purinoceptor/G protein-coupled	*****	602697	none found
Gluamate Receptor, Ionotropic, N-Methyl-	U77783	602717	none found

D-Asp 2d; Grin2d			
Gamma-Aminobutyric Acid Receptor, Pi;	U95367	602729	none found
Gatap			
cyclic nucleotide gated hyperpolarization activated potassium channel 1/HCN1	AF064876	602780	none found
cyclic nucleotide gated hyperpolarization activated potassium channel 2/HCN2	AF064877	602781	none found
Purnergic Receptor P2X, Ligand-Gated Ion Channel, 5; P2rx5	NM_002561	602836	none found
voltage independent neuronal sodium channel 2/ACCN2	NM_001095	602866	none found
voltage dependent potassium channel, subfamily S, member 1/KCN51	*****	602905	none found
voltage dependent potassium channel, subfamily S, member 2/KCN52	*****	602906	none found
neuronal voltage dependent calcium channel gamma subunit CACNG2	*****	602911	none found
RA related orphan	NM_0050	602943	none found

SD 4444.1

SD: 14:1:1

thyroid stimulating hormone receptor	NM_000369	603372	2 bases deleted of codon 655
thyroid stimulating hormone receptor	NM_000369	603372	C253A
thyroid stimulating hormone receptor	NM_000369	603372	duplication of nucleotides -346 to -330
thyroid stimulating hormone receptor	NM_000369	603372	G to C +3 intron 6
thyroid stimulating hormone receptor	NM_000369	603372	G-A -4 intron
thyroid stimulating hormone receptor	NM_000369	603372	TaqI
thyroid stimulating hormone receptor	NM_000369	603372	CYS41SER
thyroid stimulating hormone receptor	NM_000369	603372	LEU629PHE
thyroid stimulating hormone receptor	NM_000369	603372	SER505ASN
thyroid stimulating hormone receptor	NM_000369	603372	ALA553THR
thyroid stimulating hormone receptor	NM_000369	603372	ALA623ILE
thyroid stimulating hormone receptor	NM_000369	603372	alanine 623 to valine
thyroid stimulating hormone receptor	NM_000369	603372	ARG109GLN
thyroid stimulating hormone receptor	NM_000369	603372	Asn715Asp
thyroid stimulating hormone receptor	NM_000369	603372	Asp219Glu

thyroid stimulating hormone receptor	NM_000369	603372	ASP36HIS
thyroid stimulating hormone receptor	NM_000369	603372	ASP410ASN
thyroid stimulating hormone receptor	NM_000369	603372	ASP619GLY
thyroid stimulating hormone receptor	NM_000369	603372	ASP633HIS
thyroid stimulating hormone receptor	NM_000369	603372	asp727glu
thyroid stimulating hormone receptor	NM_000369	603372	Asp727Glu
thyroid stimulating hormone receptor	NM_000369	603372	CAG
thyroid stimulating hormone receptor	NM_000369	603372	[Glu]227CAT
thyroid stimulating hormone receptor	NM_000369	603372	[His]
thyroid stimulating hormone receptor	NM_000369	603372	CYS390TRP
thyroid stimulating hormone receptor	NM_000369	603372	CYS672TYR
thyroid stimulating hormone receptor	NM_000369	603372	GCG
thyroid stimulating hormone receptor	NM_000369	603372	[Ala]460GCA
thyroid stimulating hormone receptor	NM_000369	603372	[Ala]
thyroid stimulating hormone receptor	NM_000369	603372	GGT[Arg]201C
thyroid stimulating hormone receptor	NM_000369	603372	AT [His]
thyroid stimulating hormone receptor	NM_000369	603372	GLN324TER
thyroid stimulating hormone receptor	NM_000369	603372	ILE167ASN
thyroid stimulating hormone receptor	NM_000369	603372	leu677val
thyroid stimulating hormone receptor	NM_000369	603372	LYS183ARG

SD...41111

hormone receptor	69			Lys723 Met
thyroid stimulating	NM_0003	603372		
hormone receptor	69			
thyroid stimulating	NM_0003	603372		MET453THR
hormone receptor	69			
thyroid stimulating	NM_0003	603372		P52T
hormone receptor	69			
thyroid stimulating	NM_0003	603372		Phe197Ile
hormone receptor	69			
thyroid stimulating	NM_0003	603372		PHE525LEU
hormone receptor	69			
thyroid stimulating	NM_0003	603372		PHE631LEU
hormone receptor	69			
thyroid stimulating	NM_0003	603372		PRO162ALA
hormone receptor	69			
thyroid stimulating	NM_0003	603372		SER281ASN
hormone receptor	69			
thyroid stimulating	NM_0003	603372		SER281ILE
hormone receptor	69			
thyroid stimulating	NM_0003	603372		TRP546TER
hormone receptor	69			
thyroid stimulating	NM_0003	603372		VAL509ALA
hormone receptor	69			
type IX voltage	NM_0029	603415		
dependent sodium	77			none found
channel alpha				
subunit SCN9A				
homolog of Drosophila	AF071062	603448		none found
disinhibitor DAB1				
Gamma-Aminobutyric	Y11044	603540		none found
Acetylcholine Receptor 1;				

Gu-bri					
glutagon-like peptide 2	*****	603659		none found	
receptor:GLP2R					
Amine oxidase	AF054985	603735		none found	
(copper-containing)					
3/A:OC3					
voltage dependent	NM_0022	603787		none found	
potassium channel,	36				
subfamily F, member					
1/KCNF1					
voltage dependent	AF043472	603888		none found	
potassium channel,					
subfamily S, member					
3/B:CNK3					
inwardly rectifying	*****	603953		none found	
potassium channel,					
subfamily J, member					
14/KCNJ14					
sodium channel alpha-	U24693	603967		(GA)n	
subunit SCN4A					
sodium channel alpha-	U24693	603967		(GT)n	
subunit SCN4A					
sodium channel alpha-	U24693	603967			GLY1306ALA
subunit SCN4A					
sodium channel alpha-	U24693	603967			ALA1156THR
subunit SCN4A					
sodium channel alpha-	U24693	603967			ARG1448CYS
subunit SCN4A					
sodium channel alpha-	U24693	603967			ARG1448HIS
subunit SCN4A					
sodium channel alpha-	U24693	603967			GLY1306VAL

subunit/SCN4A	U24693	603967	ILE1160VAL
sodium channel alpha-subunit/SCN4A			
sodium channel alpha-subunit/SCN4A	U24693	603967	LEU1433ARG
sodium channel alpha-subunit/SCN4A			
sodium channel alpha-subunit/SCN4A	U24693	603967	MET1592VAL
sodium channel alpha-subunit/SCN4A			
sodium channel alpha-subunit/SCN4A	U24693	603967	SER804PHE
sodium channel alpha-subunit/SCN4A			
sodium channel alpha-subunit/SCN4A	U24693	603967	THR1313MET
sodium channel alpha-subunit/SCN4A			
sodium channel alpha-subunit/SCN4A	U24693	603967	THR704MET
sodium channel alpha-subunit/SCN4A			
sodium channel alpha-subunit/SCN4A	U24693	603967	VAL1293ILE
sodium channel alpha-subunit/SCN4A			
sodium channel alpha-subunit/SCN4A	U24693	603967	VAL1589MET
sodium channel alpha-subunit/SCN4A			
sodium channel alpha-subunit/SCN4A	U24693	603967	VAL445MET
sodium channel alpha-subunit/SCN4A			
Glutamate Receptor, Metabotropic 6/G	U82083	604096	none found
protein-coupled/Grm6			
Glutamate Receptor, Metabotropic 2/G	L35318	604099	none found
protein-coupled/ Grm2			
Glutamate Receptor, Metabotropic 4/G	X80818	604100	none found
protein-coupled/Grm4			
Glutamate Receptor, Metabotropic 7/G	X94552	604101	none found
protein-coupled/Grm7			

Glutamate Receptor, Metabotropic 5/G protein-coupled/Grm5	D28538	604102	none found
dihydrofolate reductase	J00140	126060	2 RFLP's
dihydrofolate reductase	J00140	126060	intronic
FKBP, tacrolimus binding protein, FK506-binding protein 1 (12kD)	M34539	186945	polymorphism none found
Cyclooxygenase 1 COX1	M59979	176805	none found
Cyclooxygenase 2 COX2	M90100	600262	none found
beta-synuclein [human, brain, mRNA, 730 nt]	S69965	602569	none found
histamine N- methyltransferase			A939G
histamine N- methyltransferase			Thr105Ile

Table 20. Identified
Variances in Genes or
Related Pathways
involved in the
Pharmacokinetics and
Pharmacodynamics of
Candidate Therapeutic
Interventions

3'(2'), 5'-bisphosphate	604053	NM_00608	none found
-------------------------	--------	----------	------------

nucleotidase 1/BPNT	5		
Acetylcholinesterase/A	100740	M55040	1431 C/T 446 silent
CHE			
Acetylcholinesterase/A	100740	M55040	408 G/C arg561pro
CHE			
Acetylcholinesterase/A	100740	M55040	HIS322ASN
CHE			
acyl-Coenzyme A			none found
dehydrogenase, C-4 to			
C-12 straight			
chain/ACADM			
(mitochondrial)			
ALCOHOL	103700		none found
DEHYDROGENASE			
1			
aldehyde	100650	K03001	GLU487LYS
dehydrogenase			
2/ALDH2 (liver			
mitochondria)			
aldehyde	100650	K03001	A-361G
dehydrogenase			
2/ALDH2 (liver			
mitochondria)			
aldehyde	100650	K03001	-357 G/A
dehydrogenase			
2/ALDH2 (liver			
mitochondria)			
ALDEHYDE	100670		C183T silent
DEHYDROGENASE			
5			
ALDEHYDE	100670		C257T Val<-->Ala

DEHYDROGENASE					
5					
ALDEHYDE	100670		T320G Arg<-->Leu		
DEHYDROGENASE					
5					
ALDO-KETO	600449		none found		
REDUCTASE					
FAMILY 1, MEMBER					
1; AKR1C1					
ALDO-KETO	103830		none found		
REDUCTASE					
FAMILY 1, MEMBER					
A1; AKR1A1					
ALDO-KETO	603966		none found		
REDUCTASE					
FAMILY 1, MEMBER					
C3					
Aldo-keto reductase	600451	*****	none found		
family 1, member					
C4/chlorodecone					
reductase/AKR1C4					
Aldo-keto reductase	603418	NM_00368	none found		
family 7; member		9			
A2/aflatoxin aldehyde					
reductase/AKR7A2					
anthracylcline	603234	NM_00117	none found		
resistance-related		1			
protein/ARA					
antigen peptide	170260	NM_00059			ILE333VAL
transporter 1/MHC		3			
1/TAP1					

antigen peptide transporter 1/MHC 1/TAP1	170260	NM_000593	ASP637GLY
antigen peptide transporter 1/MHC 1/TAP1	170260	NM_000593	ARG659GLN
antigen peptide transporter 1/MHC 1/TAP1	170260	NM_000593	val- leucine
antigen peptide transporter 1/MHC 1/TAP1	170260	NM_000593	silent glycine
antigen peptide transporter 1/MHC 1/TAP1	170260	NM_000593	silent glutamic acid
antigen peptide transporter 1/MHC 1/TAP1	170260	NM_000593	silent alanine
antigen peptide transporter 1/MHC 1/TAP1	170260	NM_000593	GTC-->ATC Val518Ile
antigen peptide transporter 1/MHC 1/TAP1	170260	NM_000593	G-->T promoter
antigen peptide transporter 1/MHC 1/TAP1	170260	NM_000593	10-bp insert intron 9
antigen peptide transporter 1/MHC 1/TAP1	170260	NM_000593	G-->T 80-bp 3' termination codon
antigen peptide transporter 1/MHC 1/TAP1	170260	NM_000593	dinucleotide repeat

transporter 1/MHC 1/TAP1	3	intron 3	
antigen peptide transporter 2/MHC 2/TAP2	170261 NM_00054 4		ILE379VAL
antigen peptide transporter 2/MHC 2/TAP2	170261 NM_00054 4		ALA665THR
antigen peptide transporter 2/MHC 2/TAP2	170261 NM_00054 4		GLN687TER
antigen peptide transporter 2/MHC 2/TAP2	170261 NM_00054 4		Thr374Ala
antigen peptide transporter 2/MHC 2/TAP2	170261 NM_00054 4	ACG to ACA 458Thr	
antigen peptide transporter 2/MHC 2/TAP2	170261 NM_00054 4	GGG to GGA 466Gly	
antigen peptide transporter 2/MHC 2/TAP2	170261 NM_00054 4	GTT to ATT 467Val-Ile	
antigen peptide transporter 2/MHC 2/TAP2	170261 NM_00054 4	ATG-->GTG Met577Val	
antigen peptide transporter 2/MHC 2/TAP2	170261 NM_00054 4		565 (Ala-Thr)
antigen peptide transporter 2/MHC	170261 NM_00054 4	silent codon 386	

2/TAP2

Aromatic L-Amino Acid	107930	M76180	SspI	
Decarboxylase/AADC/ dopa decarboxylase				
Aryl hydrocarbon receptor nuclear translocator- like/ARNTL	602550	NM_001178	none found	
Aryl hydrocarbon receptor nuclear translocator/ARNT	126110	NM_001668	MspI	
Aryl hydrocarbon receptor/AHR	600253	NM_001621	none found	
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_000487	A-to-G transition changed the first polyadenylation	ARG350SER
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_000487		
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_000487	IVS2DS, G-A, +1	
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_000487		PRO426LEU
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_000487		GLY99ASP
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_000487		SER96PH
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_000487	11-BP DEL, EX8	
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_000487		ILE-TO-SER, EX3

Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7	IVS7DS, G-A, +1	
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7		ARG84GLN
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7		GLY309SER
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7	-BP DEL FS105TER	
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7		GLY86ASP
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7		SER96LEU
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7		GLY122SER
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7		PRO136LEU
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7	1-BP DEL, 297C	
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7		GLY154ASP
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7		PRO155ARG
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7		PRO167ARG
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7		ASP169ASN
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7		ALA212VAL
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7		ALA224VAL
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7		PRO231THR

sulfatase/ARSA	7		
Arylsulfatase A/steroid	250100	NM_00048	ARG244CYS
sulfatase/ARSA	7		
Arylsulfatase A/steroid	250100	NM_00048	GLY245ARG
sulfatase/ARSA	7		
Arylsulfatase A/steroid	250100	NM_00048	THR274MET
sulfatase/ARSA	7		
Arylsulfatase A/steroid	250100	NM_00048	IVS4DS, G-A, +1
sulfatase/ARSA	7		
Arylsulfatase A/steroid	250100	NM_00048	ARG288CYS
sulfatase/ARSA	7		
Arylsulfatase A/steroid	250100	NM_00048	SER295TYR
sulfatase/ARSA	7		
Arylsulfatase A/steroid	250100	NM_00048	GLY325CYS
sulfatase/ARSA	7		
Arylsulfatase A/steroid	250100	NM_00048	ASP335VAL
sulfatase/ARSA	7		
Arylsulfatase A/steroid	250100	NM_00048	ARG370TRP
sulfatase/ARSA	7		
Arylsulfatase A/steroid	250100	NM_00048	ARG370GLN
sulfatase/ARSA	7		
Arylsulfatase A/steroid	250100	NM_00048	PRO377LEU
sulfatase/ARSA	7		
Arylsulfatase A/steroid	250100	NM_00048	GLU382LYS
sulfatase/ARSA	7		
Arylsulfatase A/steroid	250100	NM_00048	ARG390TRP
sulfatase/ARSA	7		
Arylsulfatase A/steroid	250100	NM_00048	PHE398DEL
sulfatase/ARSA	7		
Arylsulfatase A/steroid	250100	NM_00048	THR409ILE
sulfatase/ARSA	7		

SD-144141.1

Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7	GLN486TER
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7	THR799GLY
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7	P148L
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7	P191T
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7	R496H
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7	N350S
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7	9-bp deletion (2320del9) NlaIII1
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7	
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7	NlaIII2
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7	BsrI
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7	BamHI
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7	
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7	L428P
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7	I179S
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7	R84Q
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7	S96F
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7	S95N

sulfatase/ARSA	7			
Arylsulfatase A/steroid	250100	NM_00048	G119R	
sulfatase/ARSA	7			
Arylsulfatase A/steroid	250100	NM_00048	D152Y	
sulfatase/ARSA	7			
Arylsulfatase A/steroid	250100	NM_00048	R244H	
sulfatase/ARSA	7			
Arylsulfatase A/steroid	250100	NM_00048	S250Y	
sulfatase/ARSA	7			
Arylsulfatase A/steroid	250100	NM_00048	A314T	
sulfatase/ARSA	7			
Arylsulfatase A/steroid	250100	NM_00048	R384C	
sulfatase/ARSA	7			
Arylsulfatase A/steroid	250100	NM_00048	R496H	
sulfatase/ARSA	7			
Arylsulfatase A/steroid	250100	NM_00048	K367N	
sulfatase/ARSA	7			
Arylsulfatase A/steroid	250100	NM_00048	leu76pro	
sulfatase/ARSA	7			
Arylsulfatase A/steroid	250100	NM_00048	A2725G	
sulfatase/ARSA	7			
Arylsulfatase A/steroid	250100	NM_00048	A1788G	
sulfatase/ARSA	7			
Arylsulfatase A/steroid	250100	NM_00048	D255H	
sulfatase/ARSA	7			
Arylsulfatase A/steroid	250100	NM_00048	287 C-->T	
sulfatase/ARSA	7			
Arylsulfatase A/steroid	250100	NM_00048	1524+95 A-->G	
sulfatase/ARSA	7			
Arylsulfatase A/steroid	250100	NM_00048	Q190-->H	
sulfatase/ARSA	7			

Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7	A1788G
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7	A2723G
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7	C2330T
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7	11-bp deletion in exon 8
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7	A1049G
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7	TaqI
Arylsulfatase A/steroid sulfatase/ARSA	250100	NM_00048 7	BamHI
Arylsulfatase B/steroid sulfatase/ARSB	253200	NM_00004 6	GLY137VAL
Arylsulfatase B/steroid sulfatase/ARSB	253200	NM_00004 6	CYS117ARG
Arylsulfatase B/steroid sulfatase/ARSB	253200	NM_00004 6	LEU236PRO
Arylsulfatase B/steroid sulfatase/ARSB	253200	NM_00004 6	CYS405TYR
Arylsulfatase B/steroid sulfatase/ARSB	253200	NM_00004 6	1-BP DEL frameshift
Arylsulfatase B/steroid sulfatase/ARSB	253200	NM_00004 6	743C DEL frameshift
Arylsulfatase B/steroid sulfatase/ARSB	253200	NM_00004 6	11-BP DEL
Arylsulfatase B/steroid sulfatase/ARSB	253200	NM_00004 6	G302R
Arylsulfatase B/steroid sulfatase/ARSB	253200	NM_00004 6	Q456X

sulfatase/ARSB	253200	NM_000046	A1191G	
Arylsulfatase B/steroid sulfatase/ARSB	253200	NM_000046		
Arylsulfatase B/steroid sulfatase/ARSB	253200	NM_000046		*534Q
Arylsulfatase B/steroid sulfatase/ARSB	253200	NM_000046		R160*
Arylsulfatase B/steroid sulfatase/ARSB	253200	NM_000046		R160Q
Arylsulfatase B/steroid sulfatase/ARSB	253200	NM_000046		7-bp del frameshift
Arylsulfatase B/steroid sulfatase/ARSB	253200	NM_000046		deletion (delta G237-C243)
Arylsulfatase B/steroid sulfatase/ARSB	253200	NM_000046		R152W
Arylsulfatase B/steroid sulfatase/ARSB	253200	NM_000046		arg144gly
Arylsulfatase B/steroid sulfatase/ARSB	253200	NM_000046		arg192cys
Arylsulfatase B/steroid sulfatase/ARSB	253200	NM_000046		pro321leu
Arylsulfatase B/steroid sulfatase/ARSB	253200	NM_000046		insertion between T1284 and G1285
Arylsulfatase B/steroid sulfatase/ARSB	253200	NM_000046		deletion C1577
Arylsulfatase B/steroid sulfatase/ARSB	253200	NM_000046		T1600C
Arylsulfatase C, isozyme s/steroid sulfatase/ARCS1	308100	NM_0000351		TRP372ARG
Arylsulfatase C,	308100	NM_000035		CYS446TYR

isozyme s/steroid sulfatase/ARCS1	308100	NM_00035 1	SER341LEU
isozyme s/steroid sulfatase/ARCS1	308100	NM_00035 1	TRP372PRO
Arylsulfatase C, isozyme s/steroid sulfatase/ARCS1	308100	NM_00035 1	HIS444ARG
Arylsulfatase C, isozyme s/steroid sulfatase/ARCS1	308100	NM_00035 1	19-bp insertion 1477 intron/exon 18
Arylsulfatase D/steroid sulfatase/ARSD	300002	*****	none found
Arylsulfatase E/steroid sulfatase/ARSE	300180	NM_00004 7	ARG12SER
Arylsulfatase E/steroid sulfatase/ARSE	300180	NM_00004 7	GLY117ARG
Arylsulfatase E/steroid sulfatase/ARSE	300180	NM_00004 7	ARG111PRO
Arylsulfatase E/steroid sulfatase/ARSE	300180	NM_00004 7	GLY137VAL
Arylsulfatase E/steroid sulfatase/ARSE	300180	NM_00004 7	GLY245ARG
Arylsulfatase E/steroid sulfatase/ARSE	300180	NM_00004 7	CYS492TYR
Arylsulfatase F/steroid sulfatase/ARSF	300003	NM_00404 2	none found
bile salt export	603201	NM_00374	ARG575TER

SD-144141.1

butyrylcholinesterase 1/serum cholinesterase 1/BCHE1	177400	NM_00005 5	G365R
butyrylcholinesterase 1/serum cholinesterase 1/BCHE1	177400	NM_00005 5	Q119X
butyrylcholinesterase 1/serum cholinesterase 1/BCHE1	177400	NM_00005 5	R515C
butyrylcholinesterase 1/serum cholinesterase 1/BCHE1	177400	NM_00005 5	GLU497VAL
butyrylcholinesterase 1/serum cholinesterase 1/BCHE1	177400	NM_00005 5	THR243MET
butyrylcholinesterase 1/serum cholinesterase 1/BCHE1	177400	NM_00005 5	GGT-to-GGAG Gly 117 Frameshift
butyrylcholinesterase 1/serum cholinesterase 1/BCHE1	177400	NM_00005 5	Gly115 by Asp
butyrylcholinesterase 1/serum cholinesterase 1/BCHE1	177400	NM_00005 5	342-bp Alu in exon two
butyrylcholinesterase 1/serum cholinesterase 1/BCHE1	177400	NM_00005 5	209 A/G Asp-70 to Gly
butyrylcholinesterase 1/serum cholinesterase 1/BCHE1	177400	NM_00005 5	
CARBOXYLESTERA	114835		none found

SE 1; CES1

Catechol-O-Methyltransferase	116790	M58525	BglI	
Catechol-O-Methyltransferase	116790	M58525	186C > T at exon 3	
Catechol-O-Methyltransferase	116790	M58525	408C > G at exon 4	
Catechol-O-Methyltransferase	116790	M58525	472G > A at exon 4	
Catechol-O-Methyltransferase	116790	M58525	597G > A at exon 5	
Catechol-O-Methyltransferase	116790	M58525	821-827insC at the 3'	
Catechol-O-Methyltransferase	116790	M58525		Val158-->Met
Catechol-O-Methyltransferase	116790	M58525	NlaIII	
Catechol-O-Methyltransferase	116790	M58525	MspI	
Catechol-O-Methyltransferase	116790	M58525		val-108-met
Catechol-O-Methyltransferase	116790	M58525	G/A1947	
Catechol-O-Methyltransferase	116790	M58525	C256G	silent
class I aldehyde dehydrogenase	100640	M26761		none found
cytochrome P450 aromatase (CYP19)	107910	X13589	(TTTA)n in intron 5	
cytochrome P450 aromatase (CYP19)	107910	X13589	1-BP DEL, 408C	frameshift

cytochrome P450 aromatase (CYP19)	107910	X13589	G-->A at Val80 silent
cytochrome P450 aromatase (CYP19)	107910	X13589	G-1094 -A ARG365GLN
cytochrome P450 aromatase (CYP19)	107910	X13589	G-to-A Val370-to-Met
cytochrome P450 aromatase (CYP19)	107910	X13589	GT to AT exon and intron 3
cytochrome P450 aromatase (CYP19)	107910	X13589	splice donor 29 extra amino (GT>GC) of intron 6 acids
cytochrome P450 aromatase (CYP19)	107910	X13589	Arg264cys
cytochrome P450 aromatase (CYP19)	107910	X13589	ARG375CYS
cytochrome P450 aromatase (CYP19)	107910	X13589	ARG435CYS
cytochrome P450 aromatase (CYP19)	107910	X13589	CYS437TYR
cytochrome P450, subfamily I, polypeptide 1 (aryl hydrocarbon oxidase)/CYP1A1	108330	NM_00049 9	cATT-GTT Ile462Val
cytochrome P450, subfamily I, polypeptide 1 (aryl hydrocarbon oxidase)/CYP1A1	108330	NM_00049 9	MspI
cytochrome P450, subfamily I, polypeptide 1 (aryl hydrocarbon oxidase)/CYP1A1	108330	NM_00049 9	T6235C

hydrocarbon oxidase)/CYP1A1 cytochrome P450, subfamily I, polypeptide 1 (aryl hydrocarbon oxidase)/CYP1A1	108330	NM_00049 ₉	A4889G
cytochrome P450, subfamily I, polypeptide 1 (aryl hydrocarbon oxidase)/CYP1A1	108330	NM_00049 ₉	T5639C
cytochrome P450, subfamily I, polypeptide 1 (aryl hydrocarbon oxidase)/CYP1A1	108330	NM_00049 ₉	C4887A
cytochrome P450, subfamily I, polypeptide 1 (aryl hydrocarbon oxidase)/CYP1A1	108330	NM_00049 ₉	C(-459)T
cytochrome P450, subfamily I, polypeptide 1 (aryl hydrocarbon oxidase)/CYP1A1	108330	NM_00049 ₉	G(-469)A
cytochrome P450, subfamily I, polypeptide 1 (aryl hydrocarbon oxidase)/CYP1A1	108330	NM_00049 ₉	C(4151)T)

oxidase)/CYP1A1 cytochrome P450, subfamily I, polypeptide 1 (aryl hydrocarbon oxidase)/CYP1A1 cytochrome P450, subfamily I, polypeptide 2 (phenacetin metabolism)/CYP1A2 cytochrome P450, subfamily I, polypeptide 2 (phenacetin metabolism)/CYP1A2 cytochrome P450, subfamily I, polypeptide 2 (phenacetin metabolism)/CYP1A2 cytochrome P450, subfamily I, polypeptide 2 (phenacetin metabolism)/CYP1A2 cytochrome P450, subfamily IB, polypeptide 1 (dioxin inducible)/CYP1B1 cytochrome P450, subfamily IB, polypeptide 1 (dioxin inducible)/CYP1B1 cytochrome P450, subfamily IB,	108330	NM_00049 9	HinCII	
	124060	AH002667	C-->A polymorphism in intron 1	
	124060	AH002667	G->A -2964	
	124060	AH002667	F21L	
	601771	NM_00010 4	deletion 1410 to frameshift 1422	
	601771	NM_00010 4	insertion between frameshift 1209 and 1214	
	601771	NM_00010 4	GLY61GLU	

polypeptide 1 (dioxin inducible)/CYP1B1 cytochrome P450, subfamily IB,	601771	NM_000104	1546DUP10 frameshift
polypeptide 1 (dioxin inducible)/CYP1B1 cytochrome P450, subfamily IB,	601771	NM_000104	GLY365TRP
polypeptide 1 (dioxin inducible)/CYP1B1 cytochrome P450, subfamily IB,	601771	NM_000104	ARG469TRP
polypeptide 1 (dioxin inducible)/CYP1B1 cytochrome P450, subfamily IB,	601771	NM_000104	ASP374ASN
polypeptide 1 (dioxin inducible)/CYP1B1 cytochrome P450, subfamily IB,	601771	NM_000104	LYS387GLU
polypeptide 1 (dioxin inducible)/CYP1B1 cytochrome P450, subfamily IB,	601771	NM_000104	432 (Val-->Leu)
polypeptide 1 (dioxin inducible)/CYP1B1 cytochrome P450, subfamily IB,	601771	NM_000104	453 (Asn-->Ser)
polypeptide 1 (dioxin inducible)/CYP1B1 cytochrome P450,	123960	X13897	Xmnl

subfamily II, polypeptide 1 (phenobarbital inducible)/CYP2A cytochrome P450, subfamily IIA, polypeptide 6 (coumarin-7- hydroxylase)/CYP2A6	122720	NM_00076 _2	LEU160HIS
cytochrome P450, subfamily IIA, polypeptide 6 (coumarin-7- hydroxylase)/CYP2A6	122720	NM_00076 _2	CYP2A6 null
cytochrome P450, subfamily IIA, polypeptide 6 (coumarin-7- hydroxylase)/CYP2A6	122720	NM_00076 _2	Ddel
cytochrome P450, subfamily IIB (phenobarbital inducible)/CYP2B cytochrome P450, subfamily IIC, polypeptide 18/CYP2C18	123930	M29874	none found
cytochrome P450, subfamily IIC, polypeptide 18/CYP2C18	601131	*****	T204 --> A
cytochrome P450, subfamily IIC, polypeptide 18/CYP2C18	601131	*****	A-460 --> T

cytochrome P450, subfamily IIC, polypeptide 18/CYP2C18	601131	*****	Ddel	
cytochrome P450, subfamily IIC, polypeptide 18/CYP2C18	601131	*****		Thr385Met
cytochrome P450, subfamily IIC, polypeptide 19 (mephenytoin 4- hydroxylase)/CYP2C1 9	124020	NM_00076 9	40-BP DEL	
cytochrome P450, subfamily IIC, polypeptide 19 (mephenytoin 4- hydroxylase)/CYP2C1 9	124020	NM_00076 9		ARG433TRP
cytochrome P450, subfamily IIC, polypeptide 9 (hydroxylation of tolbutamide)/CYP2C9	601129	*****		
cytochrome P450, subfamily IIC, polypeptide 9	601130	*****		ILE359LEU
cytochrome P450, subfamily IIC, polypeptide 9	601130	*****		ARG144CYS

(hydroxylation of tolbutamide)/CYP2C9 cytochrome P450, subfamily IIC, polypeptide 9 (hydroxylation of tolbutamide)/CYP2C9	601130	*****	Tyr358/Cys
cytochrome P450, subfamily IIC, polypeptide 9 (hydroxylation of tolbutamide)/CYP2C9	601130	*****	Gly417/Asp
cytochrome P450, subfamily IID, polypeptide 6 (debrisoquine hydroxylation)/CYP2D 6	124030	NM_00010 6	G>C Glutamine intron splice site Histidine (splicing defect; does not splice intron at 3' site)
cytochrome P450, subfamily IID, polypeptide 6 (debrisoquine hydroxylation)/CYP2D 6	124030	NM_00010 6	G>A Glycine intron splice site Arginine (splicing defect; does not splice intron at 3' site)
cytochrome P450, subfamily IID, polypeptide 6 (debrisoquine hydroxylation)/CYP2D 6	124030	NM_00010 6	G>C Valine 136 Valine
cytochrome P450, subfamily IID, polypeptide 6 (debrisoquine hydroxylation)/CYP2D 6	124030	NM_00010	G>C Serine 486

subfamily IID, polypeptide 6 (debrisoquine hydroxylation)/CYP2D 6	124030	NM_00010 6	Threonine
cytochrome P450, subfamily IID, polypeptide 6 (debrisoquine hydroxylation)/CYP2D 6	124030	NM_00010 6	insertion Arginine (A)>deletion (A) Glycine (frameshift - premature stop next codon)
cytochrome P450, subfamily IID, polypeptide 6 (debrisoquine hydroxylation)/CYP2D 6	124030	NM_00010 6	A>C Histidine 324 Proline
cytochrome P450, subfamily IID, polypeptide 6 (debrisoquine hydroxylation)/CYP2D 6	124030	NM_00010 6	G>T Glycine 169 Stop Codon
cytochrome P450, subfamily IID, polypeptide 6 (debrisoquine hydroxylation)/CYP2D 6	124030	NM_00010 6	G>A Glycine 42 Arginine
cytochrome P450, subfamily IID, polypeptide 6 (debrisoquine hydroxylation)/CYP2D 6	124030	NM_00010 6	insertion Tryptophan (T)>deletion (T) Glycine

polypeptide 6 (debrisoquine hydroxylation)/CYP2D 6			(frameshift - premature stop at next codon)
cytochrome P450, subfamily IID, polypeptide 6 (debrisoquine hydroxylation)/CYP2D 6	124030	NM_00010 6	C>T Arginine 296 Cysteine
cytochrome P450, subfamily IID, polypeptide 6 (debrisoquine hydroxylation)/CYP2D 6	124030	NM_00010 6	C>T Proline 34 Serine
cytochrome P450, subfamily IID, polypeptide 6 (debrisoquine hydroxylation)/CYP2D 6	124030	NM_00010 6	Deletion Leucine (T)>Insertion (T) Leucine (frameshift - premature stop)
cytochrome P450, subfamily IID, polypeptide 6 (debrisoquine hydroxylation)/CYP2D 6	124030	NM_00010 6	G>A Serine 401 Serine
cytochrome P450, subfamily IID, polypeptide 6	124030	NM_00010 6	G AA>deletion Lysine 281 Lysine deletion

(debrisoquine hydroxylation)/CYP2D 6	124030	NM_00010 6	A>G Histidine 94 Arginine
cytochrome P450, subfamily IID, polypeptide 6 (debrisoquine hydroxylation)/CYP2D 6	124030	NM_00010 6	T>C Leucine 421 Proline
cytochrome P450, subfamily IID, polypeptide 6 (debrisoquine hydroxylation)/CYP2D 6	124030	NM_00010 6	AG A>deletion Lysine 281 Lysine deletion
cytochrome P450, subfamily IID, polypeptide 6 (debrisoquine hydroxylation)/CYP2D 6	124030	NM_00010 6	C>G Threonine 98 Threonine
cytochrome P450, subfamily IID, polypeptide 6 (debrisoquine hydroxylation)/CYP2D 6	124030	NM_00010 6	C>G Leucine 91 Valine

hydroxylation)/CYP2D 6	124030	NM_00010 6	G>A Glycine 212 Glutamic acid
cytochrome P450, subfamily IID, polypeptide 6 (debrisoquine hydroxylation)/CYP2D 6	124030	NM_00010 6	C>T Phenylalanine 112 Phenylalanine
cytochrome P450, subfamily IID, polypeptide 6 (debrisoquine hydroxylation)/CYP2D 6	124040	J02843	(GGAT)n.(CCTA)n repeat element intron
cytochrome P450, subfamily IIE (ethanol inducible)/CYP2E	124040	J02843	MspI
cytochrome P450, subfamily IIE (ethanol inducible)/CYP2E	124040	J02843	PstI
cytochrome P450, subfamily IIE (ethanol inducible)/CYP2E	124040	J02843	RsaI
cytochrome P450, subfamily IIE (ethanol inducible)/CYP2E	124040	J02843	XmnI
cytochrome P450, subfamily IIE (ethanol inducible)/CYP2E	124040	J02843	Taq I

inducible)/CYP2E cytochrome P450, subfamily IIF (ethoxycoumarin monooxygenase), polypeptide 1/CYP2F1	124070	NM_00077 4	none found	
cytochrome P450, subfamily IIIA (niphedipine oxidase), polypeptide 3/CYP3A3	124010	NM_00077 6	a-g PROMOTER	
cytochrome P450, subfamily IIIA (niphedipine oxidase), polypeptide 3/CYP3A3	124010	NM_00077 6	-292 a-g	
cytochrome P450, subfamily IIIA (niphedipine oxidase), polypeptide 3/CYP3A3	124010	NM_00077 6		Thr431Ile
cytochrome P450, subfamily IIIA (niphedipine oxidase), polypeptide 3/CYP3A3	124010	NM_00077 6		Trp392Val
cytochrome P450, subfamily IIIA (niphedipine oxidase), polypeptide 3/CYP3A3	124010	NM_00077 6		Ile224 replacing Thr224-Val225
Dehydroepiandrosteron e (DHEA)-preferring sulfotransferase, family 2A, member 1/SULT2A1	125263	NM_00316 7		Met 57 --> Thr

Dehydroepiandrosterone (DHEA)-preferring sulfotransferase, family 2A, member 1/SULT2A1	125263	NM_003167	Glu 186 --> Val
Dihydrolipoamide dehydrogenase (E3 component of pyruvate dehydrogenase complex, 2-oxo-glutarate complex, branched chain keto acid dehydrogenase complex)	246900	J03490	LYS37GLU
Dihydrolipoamide dehydrogenase (E3 component of pyruvate dehydrogenase complex, 2-oxo-glutarate complex, branched chain keto acid dehydrogenase complex)	246900	J03490	PRO453LEU
Dihydrolipoamide dehydrogenase (E3 component of pyruvate dehydrogenase complex, 2-oxo-glutarate complex, branched chain keto acid dehydrogenase complex)	246900	J03490	1-BP INS frameshift

complex) Dihydrolipoamide dehydrogenase (E3 component of pyruvate dehydrogenase complex, 2-oxo- glutarate complex, branched chain keto acid dehydrogenase complex)	246900	J03490	GLY229CYS
Dihydrolipoamide dehydrogenase (E3 component of pyruvate dehydrogenase complex, 2-oxo- glutarate complex, branched chain keto acid dehydrogenase complex)	246900	J03490	Y35X
Dihydrolipoamide dehydrogenase (E3 component of pyruvate dehydrogenase complex) Dihydrolipoamide dehydrogenase (E3 component of pyruvate dehydrogenase complex, 2-oxo- glutarate complex, branched chain keto acid dehydrogenase complex)	246900	J03490	R460G
Dihydrolipoamide S- acetyltransferase (E2 component of pyruvate	245349	AF001437	85-BP DEL

dehydrogenase complex)				
Dihydrolipoamide S-acetyltransferase (E2 component of pyruvate dehydrogenase complex)	245349	AF001437	69-BP DEL	
Dihydrolipoamide S-acetyltransferase (E2 component of pyruvate dehydrogenase complex)	245349	AF001437	4-BP DEL	
dihydropyrimidine dehydrogenase DPD	274270	U09178	deltaC1897	
dihydropyrimidine dehydrogenase DPD	274270	U09178	Arg21Gln	
dihydropyrimidine dehydrogenase DPD	274270	U09178	Val335Leu	
dihydropyrimidine dehydrogenase DPD	274270	U09178	Glu386Ter	
dihydropyrimidine dehydrogenase DPD	274270	U09178	165-BP DEL	
dihydropyrimidine dehydrogenase DPD	274270	U09178	Ser534Asn	
dihydropyrimidine dehydrogenase DPD	274270	U09178	Ile543Val	
dihydropyrimidine dehydrogenase DPD	274270	U09178	Val732Ile	
dihydropyrimidine dehydrogenase DPD	274270	U09178	4-BP DEL 296 to 299 (TCAT)	
dihydropyrimidine dehydrogenase DPD	274270	U09178	1-BP DEL, 1897C Frameshift	

dehydrogenase DPD	274270	U09178	ARG886HIS
dihydropyrimidine			
dehydrogenase DPD	274270	U09178	CYS29ARG
dihydropyrimidine			
dehydrogenase DPD	274270	U09178	ASP974VAL
dihydropyrimidine			
dehydrogenase DPD	126455	L24178	5' TaqI RFLP
Dopamine Transporter/ DAT1			
Dopamine Transporter/ DAT1	126455	L24178	9-repeat allele
Dopamine Transporter/ DAT1	126455	L24178	40-bp VNTR in the 3'-untranslated
eosinophil peroxidase/EPX	131399		ARG286HIS
eosinophil peroxidase/EPX	131399		INS G, NT1537
epoxide hydrolase 1/EPHX1 (microsomal)	132810	NM_000120	TYR113HIS
epoxide hydrolase 1/EPHX1 (microsomal)	132810	NM_000120	Exon 3 T to C
epoxide hydrolase 1/EPHX1 (microsomal)	132810	NM_000120	His/Arg 139
epoxide hydrolase 2/EPHX2 (cytosolic)	132811	*****	none found
ESTERASE A-4	133220		none found
ESTERASE A-5; ESA5	133230		none found

ESTERASE B	133260		none found	
ESTERASE B3; ESB3	133290		none found	
ESTERASE C	133270		none found	
Estrogen-preferring sulfotransferase/STE	600043	NM_00542_0	none found	
familial intrahepatic cholestasis 1/FIC1	602397	NM_00560_3		GLY308VAL
familial intrahepatic cholestasis 1/FIC1	602397	NM_00560_3		GLY892ARG
familial intrahepatic cholestasis 1/FIC1	602397	NM_00560_3		LEU288SER
familial intrahepatic cholestasis 1/FIC1	602397	NM_00560_3	2097T-C, +2 splice variant	
familial intrahepatic cholestasis 1/FIC1	602397	NM_00560_3		1.4-KB DEL
familial intrahepatic cholestasis 1/FIC1	602397	NM_00560_3		ILE661THR
familial intrahepatic cholestasis 1/FIC1	602397	NM_00560_3	9-BP DEL deletion GNR (795-797)	
folypolyglutamate synthetase FPGS	136510	M98045	none found	
gamma-glutamyl hydrolase GGH	601509	U55206	none found	
GAMMA- GLUTAMYLTRANSF ERASE 2	137181		none found	
Glucose-6-phosphate dehydrogenase	305900	X03674		ASN126ASP
Glucose-6-phosphate dehydrogenase	305900	X03674		VAL68MET
Glucose-6-phosphate	305900	X03674		ASN126ASP

dehydrogenase	305900	X03674	ALA335THR
Glucose-6-phosphate	305900	X03674	GLU156LYS
dehydrogenase	305900	X03674	GLY163SER
Glucose-6-phosphate	305900	X03674	SER188PHE
dehydrogenase	305900	X03674	ASP58ASN
Glucose-6-phosphate	305900	X03674	ARG393HIS
dehydrogenase	305900	X03674	GLY447ARG
Glucose-6-phosphate	305900	X03674	ASP282HIS
dehydrogenase	305900	X03674	PHE216LEU
Glucose-6-phosphate	305900	X03674	LYS386GLU
dehydrogenase	305900	X03674	ARG387HIS
Glucose-6-phosphate	305900	X03674	CYS385ARG
dehydrogenase	305900	X03674	GLY410CYS
Glucose-6-phosphate	305900	X03674	ARG285HIS
dehydrogenase	305900	X03674	NT1116, G-A
Glucose-6-phosphate	305900	X03674	
dehydrogenase	305900	X03674	

Glucose-6-phosphate dehydrogenase	305900	X03674	NT1311, C-T	
Glucose-6-phosphate dehydrogenase	305900	X03674	EX6, -60, C-G	
Glucose-6-phosphate dehydrogenase	305900	X03674		ARG454HIS
Glucose-6-phosphate dehydrogenase	305900	X03674		ARG459LEU
Glucose-6-phosphate dehydrogenase	305900	X03674		GLU398LYS
Glucose-6-phosphate dehydrogenase	305900	X03674		ASP181VAL
Glucose-6-phosphate dehydrogenase	305900	X03674		ASN126ASP
Glucose-6-phosphate dehydrogenase	305900	X03674		VAL213LEU
Glucose-6-phosphate dehydrogenase	305900	X03674		ARG393HIS
Glucose-6-phosphate dehydrogenase	305900	X03674		VAL291MET
Glucose-6-phosphate dehydrogenase	305900	X03674		ARG227LEU
Glucose-6-phosphate dehydrogenase	305900	X03674		LEU323PRO
Glucose-6-phosphate dehydrogenase	305900	X03674		ARG463HIS
Glucose-6-phosphate dehydrogenase	305900	X03674		ASN363LYS
Glucose-6-phosphate dehydrogenase	305900	X03674		ARG198CYS
Glucose-6-phosphate dehydrogenase	305900	X03674		SER106CYS

dehydrogenase	305900	X03674	ARG182TRP
Glucose-6-phosphate dehydrogenase	305900	X03674	ARG198CYS
Glucose-6-phosphate dehydrogenase	305900	X03674	ASN165ASP
Glucose-6-phosphate dehydrogenase	305900	X03674	ARG198PRO
Glucose-6-phosphate dehydrogenase	305900	X03674	ARG227GLN
Glucose-6-phosphate dehydrogenase	305900	X03674	PRO353SER
Glucose-6-phosphate dehydrogenase	305900	X03674	ARG387CYS
Glucose-6-phosphate dehydrogenase	305900	X03674	VAL394LEU
Glucose-6-phosphate dehydrogenase	305900	X03674	GLY410ASP
Glucose-6-phosphate dehydrogenase	305900	X03674	ARG439PRO
Glucose-6-phosphate dehydrogenase	305900	X03674	ILE35DEL
Glucose-6-phosphate dehydrogenase	305900	X03674	GLU317LYS
Glucose-6-phosphate dehydrogenase	305900	X03674	ILE48THR
Glucose-6-phosphate dehydrogenase	305900	X03674	HIS32ARG
Glucose-6-phosphate dehydrogenase	305900	X03674	GLY131VAL

Glucose-6-phosphate dehydrogenase	305900	X03674	LEU342PHE
Glucose-6-phosphate dehydrogenase	305900	X03674	ALA44GLY
Glucose-6-phosphate dehydrogenase	305900	X03674	PHE173LEU
Glucose-6-phosphate dehydrogenase	305900	X03674	ASP181VAL
Glucose-6-phosphate dehydrogenase	305900	X03674	PRO467ARG
Glucose-6-phosphate dehydrogenase	305900	X03674	ALA361VAL
Glucose-6-phosphate dehydrogenase	305900	X03674	24-BP DEL, NT953
Glucose-6-phosphate dehydrogenase	305900	X03674	Pro172-->Ser
Glucose-6-phosphate dehydrogenase	305900	X03674	R459L
Glucose-6-phosphate dehydrogenase	305900	X03674	R463H
Glucose-6-phosphate dehydrogenase	305900	X03674	C-->T 563
Glucose-6-phosphate dehydrogenase	305900	X03674	376A-->G
Glucose-6-phosphate dehydrogenase	305900	X03674	202G-->A
Glucose-6-phosphate dehydrogenase	305900	X03674	680G-->T
Glucose-6-phosphate dehydrogenase	305900	X03674	968T-->C
Glucose-6-phosphate dehydrogenase	305900	X03674	563C-->T

dehydrogenase	305900	X03674	202G-->A	
Glucose-6-phosphate dehydrogenase	305900	X03674	1311C-->T	
Glucose-6-phosphate dehydrogenase	305900	X03674	406 C-->T	
Glucose-6-phosphate dehydrogenase	305900	X03674	1155 C-->G	
Glucose-6-phosphate dehydrogenase	305900	X03674	185 C-->T, 62 Pro-->Phe	
Glucose-6-phosphate dehydrogenase	305900	X03674	695 G-->A	
Glucose-6-phosphate dehydrogenase	305900	X03674	1387 C-->T 463 Arg-->Cys	
Glucose-6-phosphate dehydrogenase	305900	X03674	1246 G-->A	
Glucose-6-phosphate dehydrogenase	305900	X03674	1160 G-->A	
Glucose-6-phosphate dehydrogenase	305900	X03674	Bcl I	
Glucose-6-phosphate dehydrogenase	305900	X03674	202 G-->A	
Glucose-6-phosphate dehydrogenase	305900	X03674	335 Ala-->Thr	
Glucose-6-phosphate dehydrogenase	305900	X03674	G-->T at nt 1376	
Glucose-6-phosphate dehydrogenase	305900	X03674	G-->A at 1388	
Glucose-6-phosphate dehydrogenase	305900	X03674	A-->G at nt 95	

Glucose-6-phosphate dehydrogenase	305900	X03674	A209G
Glucose-6-phosphate dehydrogenase	305900	X03674	493 A-->G
Glucose-6-phosphate dehydrogenase	305900	X03674	592 C-->T
Glucose-6-phosphate dehydrogenase	305900	X03674	844 G > C
Glucose-6-phosphate dehydrogenase	305900	X03674	224 T-->C
Glucose-6-phosphate dehydrogenase	305900	X03674	488 G-->A
Glucose-6-phosphate dehydrogenase	305900	X03674	833 C-->T
Glucose-6-phosphate dehydrogenase	305900	X03674	1360C-->T 454Arg-->Cys
Glucose-6-phosphate dehydrogenase	305900	X03674	383T-->C 128Leu-->Pro
Glucose-6-phosphate dehydrogenase	305900	X03674	208T-->C 70Tyr-->His
Glucose-6-phosphate dehydrogenase	305900	X03674	497G-->A 166Arg-->His
Glucose-6-phosphate dehydrogenase	305900	X03674	A-->G 1138 val380iso
Glucose-6-phosphate dehydrogenase	305900	X03674	T-->C 1139 iso380thr
Glucose-6-phosphate dehydrogenase	305900	X03674	C-->G 1177 gly393arg
Glucose-6-phosphate dehydrogenase	305900	X03674	C->T 1187
Glucose-6-phosphate dehydrogenase	305900	X03674	527A-->G

dehydrogenase					
Glucose-6-phosphate	305900	X03674	1003G-->A		
dehydrogenase					
Glucose-6-phosphate	305900	X03674	1159C-->T		
dehydrogenase					
Glucose-6-phosphate	305900	X03674	1160G-->A		
dehydrogenase					
Glucose-6-phosphate	305900	X03674	1229G-->A		
dehydrogenase					
Glucose-6-phosphate	305900	X03674	1246G-->A		
dehydrogenase					
Glucose-6-phosphate	305900	X03674	1361G-->A		
dehydrogenase					
Glucose-6-phosphate	305900	X03674	C-->T 563		
dehydrogenase					
Glucose-6-phosphate	305900	X03674	C-->T 1311		
dehydrogenase					
Glucose-6-phosphate	305900	X03674	241 C to T		
dehydrogenase					
Glucose-6-phosphate	305900	X03674	487 G-->A		
dehydrogenase					
glutathione peroxidase	138320	Y00433		P197L	
GPx1					
glutathione peroxidase	138320	Y00433	1167T/C Silent		
GPx1					
glutathione peroxidase	138319	X68314	A/T intron		
GPx2					
glutathione peroxidase	138319	X68314	TC repeats intron		
GPx2					
glutathione peroxidase	138321	X58295	none found		
GPx3					

glutathione peroxidase GPx4	138322	X71973	none found
glutathione peroxidase GPx5	603435	AJ005277	none found
Glutathione-S- transferase 1/MGST1 (microsomal)	138330	AH003674	none found
Glutathione-S- transferase 2/MGST2 (microsomal)	601733	NM_00241 3	none found
Glutathione-S- transferase 6	138391	*****	none found
glutathione-S- transferase GSTM3	138390	J05459	3bp deletion intron 6
glutathione-S- transferase GSTT1	600436	X79389	null genotype
glutathione-S- transferase GSTT2	600437	L38503	none found
Glutathione-S- transferase, alpha 1/GSTA1	138359	L13269	none found
Glutathione-S- transferase, alpha 2/GSTA2	138360	M15872	none found
Glutathione-S- transferase, kappa 1/GSTK1	602321	*****	none found
Glutathione-S- transferase, mu 1- like/GSTM1L	138270	*****	none found
Glutathione-S-	138350	J03817	gene deletion

transferase, mu 1/GSTM1	138380	NM_000848	none found	
Glutathione-S- transferase, mu 2/GSTM2 (muscle)	138333	NM_000850	none found	
Glutathione-S- transferase, mu 4/GSTM4	138385	NM_000851	none found	
Glutathione-S- transferase, mu 5/GSTM5 (brain/lung)	134660	NM_000852	ILE104VAL	
Glutathione-S- transferase, pi/GSTP1	134660	NM_000852	ALA113VAL	
Glutathione-S- transferase, pi/GSTP1	134660	NM_000852	BamHI	
Glutathione-S- transferase, pi/GSTP1	134660	NM_000852	(ATAAA)n upstream of gene	
Glutathione-S- transferase, pi/GSTP1	138610		none found	
GLYCOPROTEIN, ALPHA-I-ACID, OF SERUM, TYPE 2	602403	X92106	ILE443VAL	
H.sapiens mRNA for bleomycin hydrolase	164012	X61498		
H.sapiens mRNA for NF-kB subunit			A939G	
histamine N- methyltransferase			Thr105Ile	
histamine N- methyltransferase				
Homo sapiens ABC	MOATB	AF071202	none found	

transporter MOAT-B (MOAT-B) mRNA, complete cds	103730	M12272	ile349-to-val
Homo sapiens alcohol dehydrogenase class I gamma subunit (ADH3) mRNA, complete cds	103730	M12272	ARG271GLU
Homo sapiens gamma- glutamylcysteine synthetase light subunit mRNA, complete cds	601176	L35546	none found
Homo sapiens mRNA for 25-hydroxyvitamin D3 1-alpha- hydroxylase, complete cds	264700	AB005038	ARG107HIS
Homo sapiens mRNA for 25-hydroxyvitamin D3 1-alpha- hydroxylase, complete cds	264700	AB005038	GLY125GLU
Homo sapiens mRNA for 25-hydroxyvitamin D3 1-alpha- hydroxylase, complete cds	264700	AB005038	ARG335PRO

cds Homo sapiens mRNA for 25-hydroxyvitamin D3 1-alpha- hydroxylase, complete	264700	AB005038	PRO382SER
cds Homo sapiens mRNA for 25-hydroxyvitamin D3 1-alpha- hydroxylase, complete	264700	AB005038	1-BP DEL frameshift
cds Homo sapiens mRNA for 25-hydroxyvitamin D3 1-alpha- hydroxylase, complete	264700	AB005038	1-BP DEL, 958G
cds Homo sapiens mRNA for 25-hydroxyvitamin D3 1-alpha- hydroxylase, complete	264700	AB005038	7-BP DUP
cds Homo sapiens mRNA for carbonyl reductase 3, complete cds	603608	AB004854	none found
Homo sapiens paraoxonase 2 (PON2) mRNA, complete cds	602447	L48513	CYS311SER
Homo sapiens paraoxonase 2 (PON2) mRNA, complete cds	602447	L48513	ALA148GLY
Homo sapiens	602720	L48516	none found

paraoxonase 3 (PON3) mRNA, 3' end of cds	602239	AF005418	none found
Homo sapiens retinoic acid hydroxylase mRNA, complete cds	SMRP	AB005659	none found
Homo sapiens SMRP mRNA, complete cds	600086	U07821	none found
Human alcohol dehydrogenase (ADH7) mRNA, complete cds	103735	M68895	none found
Human alcohol dehydrogenase 6 gene, complete cds	103710	M29872	MspI
Human aldehyde dehydrogenase (ALDH8) mRNA, complete cds	601917	U37519	none found
Human aldehyde dehydrogenase 6 mRNA, complete cds	600463	U07919	none found
Human aldehyde dehydrogenase ALDH7 mRNA, complete cds	600466	U10868	none found
Human aldehyde dehydrogenase type III (ALDHIII) mRNA,	100660	M74542	none found

complete cds	138600	M13692	VAL156MET
Human alpha-1 acid glycoprotein mRNA, complete cds	138600	M13692	GLN20ARG
Human alpha-1 acid glycoprotein mRNA, complete cds	151530	M22324	none found
Human aminopeptidase N/CD13 mRNA encoding aminopeptidase N, complete cds	600338	L32179	none found
Human arylacetamide deacetylase mRNA, complete cds	114830	J04056	none found
Human carbonyl reductase mRNA, complete cds	103720	M24317	ARG47HIS
Human class I alcohol dehydrogenase (ADH2) beta-1 subunit mRNA, complete cds	103720	M24317	ARG369CYS
Human class I alcohol dehydrogenase (ADH2) beta-1 subunit mRNA, complete cds	103740	M15943	-75A-->C
Human class II alcohol dehydrogenase (ADH4) pi subunit mRNA, complete cds			

Human factor KBF1 mRNA, complete cds	164011	M55643	(CA)n	
Human fatty aldehyde dehydrogenase (FALDH) mRNA, complete cds	270200	L47162	1-BP DEL, 525T	
Human fatty aldehyde dehydrogenase (FALDH) mRNA, complete cds	270200	L47162	1-BP DEL, 808G	
Human fatty aldehyde dehydrogenase (FALDH) mRNA, complete cds	270200	L47162	3-BP DEL/21-BP INS	
Human fatty aldehyde dehydrogenase (FALDH) mRNA, complete cds	270200	L47162		ALA314GLY
Human fatty aldehyde dehydrogenase (FALDH) mRNA, complete cds	270200	L47162		PRO315ALA
Human fatty aldehyde dehydrogenase (FALDH) mRNA, complete cds	270200	L47162		CYS214TYR
Human fatty aldehyde dehydrogenase (FALDH) mRNA, complete cds	270200	L47162		PRO315SER
Human fatty aldehyde dehydrogenase (FALDH) mRNA, complete cds	270200	L47162	2-BP DEL, 1297GA frameshift	

SD-144141.1

dehydrogenase (FALDH) mRNA, complete cds	270200	L47162	5-BP INS, NT1311	
Human fatty aldehyde dehydrogenase (FALDH) mRNA, complete cds	602733	U34252		CYS115SER
Human gamma- aminobutyraldehyde dehydrogenase mRNA, complete cds	230450	M90656	A-->T 1109 His370Leu	
Human gamma- glutamylcysteine synthetase (GCS) mRNA, complete cds	230450	M90656	(CAGC)n 1972-1975	
Human gamma- glutamylcysteine synthetase (GCS) mRNA, complete cds	137168	M64099	none found	
Human gamma- glutnyl transpeptidase- related protein (GGT- Rel) mRNA, complete cds	601002	U34683		ARG164GLN
Human glutathione synthetase mRNA, complete cds	601002	U34683	1-BP DEL frameshift	
Human glutathione synthetase mRNA, complete cds	601002	U34683		ARG267TRP

synthetase mRNA, complete cds	601002	U34683	ARG283CYS
Human glutathione synthetase mRNA, complete cds	601002	U34683	ARG125CYS
Human glutathione synthetase mRNA, complete cds	601002	U34683	PRO314LEU
Human glutathione synthetase mRNA, complete cds	601002	U34683	6-BP DEL VAL-GLN del
Human glutathione synthetase mRNA, complete cds	601002	U34683	ASP219GLY
Human kidney mRNA for catalase	115500	X04076	IVS4, G-A, +5
Human kidney mRNA for catalase	115500	X04076	A to T -21
Human kidney mRNA for catalase	115500	X04076	C to A -20
Human kidney mRNA for catalase	115500	X04076	C to T -18
Human kidney mRNA for catalase	115500	X04076	T to C 4
Human kidney mRNA for catalase	115500	X04076	T to C 44
Human kidney mRNA for catalase	115500	X04076	T to C 49

Human kidney mRNA for catalase	115500	X04076	C to T 12
Human kidney mRNA for catalase	115500	X04076	C to A 27
Human kidney mRNA for catalase	115500	X04076	358 T-->del
Human kidney mRNA for catalase	115500	X04076	MspI
Human messenger RNA for serum albumin (HSA)	103600	V00494	ARG-2HIS
Human messenger RNA for serum albumin (HSA)	103600	V00494	ARG-1GLN
Human messenger RNA for serum albumin (HSA)	103600	V00494	ARG-1PRO
Human messenger RNA for serum albumin (HSA)	103600	V00494	ASP1VAL
Human messenger RNA for serum albumin (HSA)	103600	V00494	HIS3GLN
Human messenger RNA for serum albumin (HSA)	103600	V00494	ARG114GLY
Human messenger RNA for serum albumin (HSA)	103600	V00494	GLU119LYS
Human messenger RNA for serum albumin (HSA)	103600	V00494	ASP269GLY

albumin (HSA) Human messenger RNA for serum albumin (HSA)	103600	V00494	LYS313ASN
Human messenger RNA for serum albumin (HSA)	103600	V00494	ALA320THR
Human messenger RNA for serum albumin (HSA)	103600	V00494	ARG-2CYS
Human messenger RNA for serum albumin (HSA)	103600	V00494	GLU321LYS
Human messenger RNA for serum albumin (HSA)	103600	V00494	GLU354LYS
Human messenger RNA for serum albumin (HSA)	103600	V00494	GLU358LYS
Human messenger RNA for serum albumin (HSA)	103600	V00494	ASP365HIS
Human messenger RNA for serum albumin (HSA)	103600	V00494	LYS372GLU
Human messenger RNA for serum albumin (HSA)	103600	V00494	ASP375ASN
Human messenger RNA for serum albumin (HSA)	103600	V00494	GLU376LYS

Human messenger RNA for serum albumin (HSA)	103600	V00494	GLU382LYS
Human messenger RNA for serum albumin (HSA)	103600	V00494	GLU501LYS
Human messenger RNA for serum albumin (HSA)	103600	V00494	LYS541GLU
Human messenger RNA for serum albumin (HSA)	103600	V00494	ASP550GLY
Human messenger RNA for serum albumin (HSA)	103600	V00494	ASP563ASN
Human messenger RNA for serum albumin (HSA)	103600	V00494	GLU565LYS
Human messenger RNA for serum albumin (HSA)	103600	V00494	GLU570LYS
Human messenger RNA for serum albumin (HSA)	103600	V00494	LYS573GLU
Human messenger RNA for serum albumin (HSA)	103600	V00494	LYS574ASN
Human messenger RNA for serum albumin (HSA)	103600	V00494	IVS6, A-G, -2
Human messenger RNA for serum albumin (HSA)	103600	V00494	EX14DEL

RNA for serum albumin (HSA)	103600	V00494	LYS536GLU
Human messenger RNA for serum albumin (HSA)	103600	V00494	ARG-2CYS
Human messenger RNA for serum albumin (HSA)	103600	V00494	ARG-1LEU
Human messenger RNA for serum albumin (HSA)	103600	V00494	GLN580LYS
Human messenger RNA for serum albumin (HSA)	103600	V00494	GLU60LYS
Human messenger RNA for serum albumin (HSA)	103600	V00494	GLU82LYS
Human messenger RNA for serum albumin (HSA)	103600	V00494	ASP494ASN
Human messenger RNA for serum albumin (HSA)	103600	V00494	ASP365VAL
Human messenger RNA for serum albumin (HSA)	103600	V00494	HIS128ARG
Human messenger RNA for serum albumin (HSA)	103600	V00494	IVS13DS, G-C, +1

albumin (HSA) Human messenger RNA for serum albumin (HSA)	103600	V00494	LYS240GLU
Human messenger RNA for serum albumin (HSA)	103600	V00494	AAT267AAAT frameshift
Human messenger RNA for serum albumin (HSA)	103600	V00494	ARG218HIS
Human messenger RNA for serum albumin (HSA)	103600	V00494	HIS3TYR
Human messenger RNA for serum albumin (HSA)	103600	V00494	LYS225GLN
Human messenger RNA for serum albumin (HSA)	103600	V00494	LYS276ASN
Human messenger RNA for serum albumin (HSA)	103600	V00494	TGC567GC frameshift
Human messenger RNA for serum albumin (HSA)	103600	V00494	TYR140CYS
Human messenger RNA for serum albumin (HSA)	103600	V00494	ASP63ASN
Human messenger RNA for serum albumin (HSA)	103600	V00494	CYS177PHE

Human messenger RNA for serum albumin (HSA)	103600	V00494	GLN268ARG
Human messenger RNA for serum albumin (HSA)	103600	V00494	ASN318LYS
Human messenger RNA for serum albumin (HSA)	103600	V00494	GLU333LYS
Human messenger RNA for serum albumin (HSA)	103600	V00494	GLU376ASN
Human messenger RNA for serum albumin (HSA)	103600	V00494	GLU479LYS
Human messenger RNA for serum albumin (HSA)	103600	V00494	GLU505LYS
Human messenger RNA for serum albumin (HSA)	103600	V00494	ARG218PRO
Human messenger RNA for serum albumin (HSA)	103600	V00494	LEU66PRO
Human messenger RNA for serum albumin (HSA)	103600	V00494	Arg218His
Human messenger RNA for serum albumin (HSA)	103600	V00494	HaeIII intron 7
Human mitochondrial	600125	L13286	none found

1,25-dihydroxyvitamin D3 24-hydroxylase mRNA, complete cds Human mRNA for brain pyruvate dehydrogenase (EC 1.2.4.1)	312170	X52709	4-BP DEL	
Human mRNA for brain pyruvate dehydrogenase (EC 1.2.4.1)	312170	X52709	7-BP DEL	
Human mRNA for brain pyruvate dehydrogenase (EC 1.2.4.1)	312170	X52709		ARG378HIS
Human mRNA for brain pyruvate dehydrogenase (EC 1.2.4.1)	312170	X52709		LYS313DEL
Human mRNA for brain pyruvate dehydrogenase (EC 1.2.4.1)	312170	X52709	2-BP DEL frameshift	
Human mRNA for brain pyruvate dehydrogenase (EC 1.2.4.1)	312170	X52709	20-BP DEL, EX11DEL	
Human mRNA for brain pyruvate dehydrogenase (EC 1.2.4.1)	312170	X52709	21-BP INS	

Human mRNA for brain pyruvate dehydrogenase (EC 1.2.4.1)	312170	X52709	ARG234GLY
Human mRNA for brain pyruvate dehydrogenase (EC 1.2.4.1)	312170	X52709	ARG302CYS
Human mRNA for brain pyruvate dehydrogenase (EC 1.2.4.1)	312170	X52709	4-BP INS frameshift
Human mRNA for brain pyruvate dehydrogenase (EC 1.2.4.1)	312170	X52709	ASP258ALA
Human mRNA for brain pyruvate dehydrogenase (EC 1.2.4.1)	312170	X52709	PHE205LEU
Human mRNA for brain pyruvate dehydrogenase (EC 1.2.4.1)	312170	X52709	TYR243ASN
Human mRNA for brain pyruvate dehydrogenase (EC 1.2.4.1)	312170	X52709	ASP315ASN
Human mRNA for brain pyruvate dehydrogenase (EC 1.2.4.1)	312170	X52709	MET282LEU

1.2.4.1) Human mRNA for brain pyruvate dehydrogenase (EC 1.2.4.1)	312170	X52709	-BP INS FS141TER
Human mRNA for brain pyruvate dehydrogenase (EC 1.2.4.1)	312170	X52709	ARG10PRO
Human mRNA for brain pyruvate dehydrogenase (EC 1.2.4.1)	312170	X52709	13-BP INS, EX10
Human mRNA for brain pyruvate dehydrogenase (EC 1.2.4.1)	312170	X52709	36-BP INS
Human mRNA for dipeptidase	179780	D13138	none found
Human mRNA for glutathione reductase (EC 1.6.4.2)	138300	X15722	none found
Human mRNA for pancreatic gamma- glutamyltransferase	231950	X60069	none found
Human multidrug resistance-associated protein homolog (MRP3)	CMOAT2	U83659	none found
Human Na/taurocholate	182396	L21893	none found

cotransporting polypeptide mRNA, complete cds	Monoamine Oxidase A; MAOA	309850	M69226	23-bp VNTR
	Monoamine Oxidase A; MAOA	309850	M69226	3rd base of codon 941 941 G>T
Monoamine Oxidase A; MAOA	Monoamine Oxidase A; MAOA	309850	M69226	A1026T ProlineProline
	Monoamine Oxidase A; MAOA	309850	M69226	A1559G LysineArginine
Monoamine Oxidase A; MAOA	Monoamine Oxidase A; MAOA	309850	M69226	A385C ArginineArginine ^e
	Monoamine Oxidase A; MAOA	309850	M69226	C1410T Aspartic AcidAspartic Acid
Monoamine Oxidase A; MAOA	Monoamine Oxidase A; MAOA	309850	M69226	C886T GlutamineTermin ation codon
	Monoamine Oxidase A; MAOA	309850	M69226	C886T Glutamine296T ermination codon
Monoamine Oxidase A; MAOA	Monoamine Oxidase A; MAOA	309850	M69226	exon 14 -- RFLP (EcoRV enzyme)
	Monoamine Oxidase A; MAOA	309850	M69226	length of (CA) _n repeat
Monoamine Oxidase A; MAOA	Monoamine Oxidase A; MAOA	309850	M69226	RFLP (EcoRV enzyme)
	Monoamine Oxidase A; MAOA	309850	M69226	RFLP (Pst I)
Monoamine Oxidase A; MAOA	Monoamine Oxidase A; MAOA	309850	M69226	T891G
	Monoamine Oxidase A; MAOA	309850	M69226	

SD-144141.1

Monoamine Oxidase A; MAOA	309850	M69226	T891G Arginine	Arginine
Monoamine Oxidase B; MAOB	309860	M69177	(GT) ⁿ repeat	
Monoamine Oxidase B; MAOB	309860	M69177	36 bases upstream from intron 13-exon 14 boundary	
Monoamine Oxidase B; MAOB	309860	M69177	A at position 644 of intron 13	
Monoamine Oxidase B; MAOB	309860	M69177	G at position 644 of intron 13	
Multidrug resistance associated protein MRP1	158343	L05628	RFLP (MaeIII enzyme)	
Multidrug resistance associated protein MRP2	601107	U83659	none found	
Multidrug resistance protein MDR1	171050	X96395	HindIII	
Multidrug resistance protein MDR1	171050	X96395	Ser893Ala	
Multidrug resistance protein MDR1	171050	X96395	GLY185VAL	
Multidrug resistance protein MDR3/P- glycoprotein 3/P _g Y3	602347	X06181	none found	
Myeloperoxidase/MPO	254600		ARG569TRP	
Myeloperoxidase/MPO	254600		TYR173CYS	
Myeloperoxidase/MPO	254600		MET251THR	

myeloperoxidase/MPO	254600	G to A in the promoter -463 G/A
myeloperoxidase/MPO	254600	Dinucleotide repeat
myeloperoxidase/MPO	254600	EcoRV RFLP
myeloperoxidase/MPO	254600	PstI
N-acetyltransferase 1/arylamine acetylase	108345	NM_000662 POLYADENYLATION SIGNAL VARIANT
N-acetyltransferase 1/arylamine acetylase	108345	NM_000662 VAL149ILE
N-acetyltransferase 1/arylamine acetylase	108345	NM_000662 C1095A
N-acetyltransferase 1/arylamine acetylase	108345	NM_000662 T1088A
N-acetyltransferase 1/arylamine acetylase	108345	NM_000662 C1095A
N-acetyltransferase 1/arylamine acetylase	108345	NM_000662 9 bp deletion
N-acetyltransferase 1/arylamine acetylase	108345	NM_000662 G560A
N-acetyltransferase 1/arylamine acetylase	108345	NM_000662 C559T
N-acetyltransferase	108345	NM_000662 C190T

1/arylamide acetylase 1/NAT1	2			
N-acetyltransferase 1/arylamide acetylase 1/NAT1	108345	NM_00066 2	350-351 (GG to CC)	
N-acetyltransferase 1/arylamide acetylase 1/NAT1	108345	NM_00066 2	497-499 (GGG to CCC)	
N-acetyltransferase 1/arylamide acetylase 1/NAT1	108345	NM_00066 2	C97T	
N-acetyltransferase 1/arylamide acetylase 1/NAT1	108345	NM_00066 2	C190T	
N-acetyltransferase 1/arylamide acetylase 1/NAT1	108345	NM_00066 2	T402C	
N-acetyltransferase 1/arylamide acetylase 1/NAT1	108345	NM_00066 2	G445A	
N-acetyltransferase 1/arylamide acetylase 1/NAT1	108345	NM_00066 2	G459A	
N-acetyltransferase 1/arylamide acetylase 1/NAT1	108345	NM_00066 2	T640G	
N-acetyltransferase 1/arylamide acetylase 1/NAT1	108345	NM_00066 2	C559T	
N-acetyltransferase 1/arylamide acetylase 1/NAT1	108345	NM_00066 2	G560A	

1/NAT1	108345	NM_000662	A613G	
N-acetyltransferase 1/arylamide acetylase				
1/NAT1	108345	NM_000662	A752T	
N-acetyltransferase 1/arylamide acetylase				
1/NAT1	108345	NM_000662	T777C	
N-acetyltransferase 1/arylamide acetylase				
1/NAT1	108345	NM_000662	G781A	
N-acetyltransferase 1/arylamide acetylase				
1/NAT1	108345	NM_000662	A787G	
N-acetyltransferase 1/arylamide acetylase				
1/NAT1	108345	NM_000662		Arg187 to a stop codon
N-acetyltransferase 1/arylamide acetylase				
1/NAT1	108345	NM_000662		Arg187 to Gln
N-acetyltransferase 1/arylamide acetylase				
1/NAT1	108345	NM_000662		
N-acetyltransferase 1/arylamide acetylase				
1/NAT1	108345	NM_000662		-344 (C-->T)
N-acetyltransferase 1/arylamide acetylase				
1/NAT1	108345	NM_000662		640 T-->G Ser-->Ala
N-acetyltransferase 1/arylamide acetylase				
1/NAT1	243400	NM_000015		ARG197GLN
N-acetyltransferase 2/arylamide acetylase				
2/NAT2				

N-acetyltransferase 2/arylamine acetylase 2/NAT2	243400	NM_00001 5	ILE114THR
N-acetyltransferase 2/arylamine acetylase 2/NAT2	243400	NM_00001 5	LYS268ARG
N-acetyltransferase 2/arylamine acetylase 2/NAT2	243400	NM_00001 5	857G-A GLY-GLU
N-acetyltransferase 2/arylamine acetylase 2/NAT2	243400	NM_00001 5	191G-A Arg64-->Gln
N-acetyltransferase 2/arylamine acetylase 2/NAT2	243400	NM_00001 5	C282T (silent)
N-acetyltransferase 2/arylamine acetylase 2/NAT2	243400	NM_00001 5	T341C Ile114-->Thr
N-acetyltransferase 2/arylamine acetylase 2/NAT2	243400	NM_00001 5	481C-->T silent
N-acetyltransferase 2/arylamine acetylase 2/NAT2	243400	NM_00001 5	590 G-->A Arg197-->Gln
N-acetyltransferase 2/arylamine acetylase 2/NAT2	243400	NM_00001 5	803 A-->G Lys268-->Arg
N-acetyltransferase 2/arylamine acetylase 2/NAT2	243400	NM_00001 5	857 G-->A Gly286-->Glu
N-acetyltransferase	243400	NM_00001	C759T

2/arylamide acetylase 2/NAT2	5			
NAD(P)H menadione oxidoreductase 1, dioxin- inducible/NMOR1/diaphorase 4/DIA4	125860	NM_000903	609C>T	pro187ser
NAD(P)H menadione oxidoreductase 2, dioxin- inducible/NMOR2	160998	NM_000904	none found	
NEUROPATHY TARGET ESTERASE	603197		none found	
nicotinamide N- methyltransferase/NNMT	600008	NM_006169	eight SNPs within intron 1	
O6 alkylguanine-DNA alkyltransferase	156569	M60761	GGA to AGA	gly160arg
O6 alkylguanine-DNA alkyltransferase	156569	M60761	1034A>G	
O6 alkylguanine-DNA alkyltransferase	156569	M60761	1099C>T	
O6 alkylguanine-DNA alkyltransferase	156569	M60761	79G>T	
paraoxonase 1/PON1 (arylesterase)	168820	AH004193		GLN192ARG
paraoxonase 1/PON1 (arylesterase)	168820	AH004193		MET54LEU
paraoxonase 1/PON1 (arylesterase)	168820	AH004193		Leu55Met
paraoxonase 1/PON1	168820	AH004193	CA repeat	intron 4.

(arylesterase)	601250	none found	
PEPTIDE			
METHIONINE			
SULFOXIDE			
REDUCTASE			
Peroxisome	170998	NM_00503 ₆	none found
proliferative activated			
receptor, alpha/PPARA			
Peroxisome	600409	NM_00623 ₈	none found
proliferative activated			
receptor, delta/PPARD			
Peroxisome	601487	NM_00503 ₇	PRO115GLN
proliferative activated			
receptor, gamma/PPARG			
Peroxisome	601487	NM_00503 ₇	PRO12ALA
proliferative activated			
receptor, gamma/PPARG			
Peroxisome	601487	NM_00503 ₇	1-BP DEL, 472A Frameshift
proliferative activated			
receptor, gamma/PPARG			
Peroxisome	601487	NM_00503 ₇	GLN286PRO
proliferative activated			
receptor, gamma/PPARG			
Peroxisome	601487	NM_00503 ₇	LYS319TER
proliferative activated			
receptor, gamma/PPARG			

Peroxisome proliferative activated receptor, gamma/PPARG	601487	NM_00503 7	ARG288HIS
Phenol-preferring sulfotransferase, family 1A, member 1/SULT1A1	171150	NM_00105 5	Arg213His
Phenol-preferring sulfotransferase, family 1A, member 2/SULT1A2	601292	NM_00105 4	none found
Phenol-preferring sulfotransferase, family 1A, member 3/SULT1A3	600641	L19956	none found
phenylethanolamine N- methyltransferase/PN MT	171190	NM_00268 6	BANI
PHOSPHOADENOSI NE-	603262		none found
PHOSPHOSULFATE SYNTHETASE I	179060	M34479	none found
Pyruvate dehydrogenase (lipoamide) beta	600825	NM_00294 3	none found
RAR related orphan receptor A/RORA	602943	NM_00506 0	none found
RAR related orphan receptor C/RORC	600424	U19720	none found

RFC1

renal microsomal dipeptidase/DPEP1 (b-lactam ring hydrolysis)	179780	NM_004413	none found	
renal transport of beta-amino acids/AABT	109660		none found	
retinoic acid receptor alpha/RARA	180240	NM_000964	7-base deletion frameshift	
retinoic acid receptor alpha/RARA	180240	NM_000964	codon 411 C to T	
retinoic acid receptor alpha/RARA	180240	NM_000964		Arg272Gln
retinoic acid receptor alpha/RARA	180240	NM_000964		Met297Leu
retinoic acid receptor beta/RARB	180220	NM_000965	none found	
retinoic acid receptor gama/RARG	180190	M57707	none found	
retinoid X receptor alpha/RXRA	180245	NM_002957	none found	
retinoid X receptor beta/RXRB	180246	X66424	none found	
retinoid X receptor gamma/RXRG	180247	U38480	none found	
serotonin transporter	182138	X70697	PstI promoter 44-bp ins/del	
serotonin transporter	182138	X70697	tandem repeat close to the promoter	
serotonin transporter	182138	X70697	two polyadenylation sites	

serotonin transporter	182138	X70697	VNTR intron 2	silent
serotonin transporter	182138	X70697		polymorphism
Solute Carrier Family 1, Member 1; Slc1a1	133550	U08989	none found	
Solute Carrier Family 1, Member 2; Slc1a2	600300	U03505	none found	
Solute Carrier Family 1, Member 3; Slc1a3	600111	U03504	none found	
Solute carrier family 1, member 4/SLC1A4 (glutamate)	600229	NM_003038	none found	
Solute carrier family 1, member 5/SLC1A5 (neutral AA)	109190	AF105230	none found	
Solute carrier family 1, member 6 (GABA/GLU)/SLC1A6	600637	NM_005071	none found	
Solute carrier family 10, member 1/SLC10A1 (taurocholate)	182396	NM_003049	none found	
Solute carrier family 10, member 2/SLC10A2 (taurocholate)	601295	NM_000452		LEU243PRO
Solute carrier family 10, member 2/SLC10A2 (taurocholate)	601295	NM_000452		THR262MET

Solute carrier family 10, member 2/SLC10A2 (taurocholate)	601295	NM_00045 2	A171S
Solute carrier family 12, member 2/SLC12A2 (dicarboxylic acids)	604148	NM_00398 4	none found
Solute carrier family 15, member 1/SLC15A1 (peptides)	600544	U13173	none found
Solute carrier family 15, member 2/SLC15A2 (peptides)	602339	S78203	none found
Solute carrier family 16, member 1/SLC16A1 (monocarboxylic acids)	600682	NM_00305 1	none found
Solute carrier family 16, member 2/SLC16A2 (monocarboxylic acids)	300095	NM_00651 7	none found
Solute carrier family 16, member 3/SLC16A3 (monocarboxylic acids)	603877	NM_00420 7	none found
Solute carrier family 16, member 4/SLC16A4 (monocarboxylic acids)	603878	*****	none found
Solute carrier family	603879	NM_00469	none found

16, member 5/SLC16A5 (monocarboxylic acids) Solute carrier family 16, member 6/SLC16A6 (monocarboxylic acids) Solute carrier family 16, member 7/SLC16A7 (monocarboxylic acids) Solute carrier family 21, member 2/SLC21A2 (prostaglandin) Solute carrier family 21, member 3/SLC21A3 (organic anion) Solute carrier family 22, member 1- like/SLC22A1 (organic cation) Solute carrier family 22, member 1- like/SLC22A1 (organic cation) Solute carrier family 22, member 1/SLC22A2 (organic cation)	603880	NM_004694	none found
	603654	AF049608	none found
	601460	NM_005630	none found
	602883	NM_005075	none found
	602631	AF037064	111-BP INS
	602631	AF037064	688G-A
	602607	NM_003058	none found

Solute carrier family 22, member 2/SLC22A2 (organic cation)	602608	NM_00305 8	
Solute carrier family 22, member 5/SLC22A5 (carnitine)	603377		113-BP DEL
Solute carrier family 22, member 5/SLC22A5 (carnitine)	603377		1-BP INS, 226C
Solute carrier family 22, member 5/SLC22A5 (carnitine)	603377		TRP132TER
Solute carrier family 22, member 5/SLC22A5 (carnitine)	603377		G-to-A transition in the last nucleotide of intron 8 1394-BP DEL
Solute carrier family 22, member 5/SLC22A5 (carnitine)	603377		19-BP INS
Solute carrier family 22, member 5/SLC22A5 (carnitine)	603377		171-BP DEL
Solute carrier family 22, member 5/SLC22A5 (carnitine)	603377		ARG282TER
Solute carrier family 22, member 5/SLC22A5 (carnitine)	603377		TYR401TER

Solute carrier family 22, member 5/SLC22A5 (carnitine)	603377	1-BP DEL, 1345G	
Solute carrier family 22, member 5/SLC22A5 (carnitine)	603377		PRO478LEU
Solute carrier family 22, member 5/SLC22A5 (carnitine)	603377		TYR211CYS
Solute carrier family 22, member 5/SLC22A5 (carnitine)	603377		Arg169Gln
Solute carrier family 25, member 1/SLC25A1 (tricarboxylic acids)	190315	X96924	none found
Solute carrier family 29 (nucleosides), member 1/SLC29A1/ENT1	602193	NM_004955	none found
Solute carrier family 29 (nucleosides), member 2/SLC29A2/ENT2	602110	X86681	none found
Solute carrier family 3 member 1/SLC3A1 (aa transporter)	104614	*****	none found
Solute carrier family 5 member 6/SLC5A6 (folate, biotin, lipoate)	604024	*****	none found
Solute carrier family 6 (GABA), member 1/SLC6A1	137165	X54673	none found

Solute carrier family 6 (betaine/GABA), member 12	603080	U27699	none found
Solute carrier family 6, member	163970	NM_00104 3	none found
5/SLC6A2/NAT1/NET 1 (glycine)	604159	NM_00421 1	none found
Solute carrier family 6, member 5/SLC6A5 (glycine)	186854	U16120	Dinucleotide repeat
Solute carrier family 6, member 6/SLC6A6 (taurine)	601019	S70612	none found
Member 9; SLC6A9 (glycine)	104615	*****	TaqI
Solute carrier family 7, member 1/SLC7A1 (cationic AA)	601872	D29990	none found
Solute carrier family 7, member 2/SLC7A2 (cationic AA)	603752	*****	none found
Solute carrier family 7, member 4/SLC7A4 (cationic AA)	600182	M80244	none found
Solute carrier family 7, member 5/SLC7A5 (neutral AA)	603593	Y18474	118I, A-T, -2 A->T
Solute carrier family 7, member 7/SLC7A7 (dibasic AA)			

Solute carrier family 7, member 7/SLC7A7 (dibasic AA)	603593	Y18474	543-BP DEL	
Solute carrier family 7, member 7/SLC7A7 (dibasic AA)	603593	Y18474	4-BP INS	
Solute carrier family 7, member 9/SLC7A9 (neutral AA)	604144	*****		VAL170MET
Solute carrier family 7, member 9/SLC7A9 (neutral AA)	604144	*****		GLY105ARG
Solute carrier family 7, member 9/SLC7A9 (neutral AA)	604144	*****		ALA182THR
Solute carrier family 7, member 9/SLC7A9 (neutral AA)	604144	*****		GLY195ARG
Solute carrier family 7, member 9/SLC7A9 (neutral AA)	604144	*****		GLY259ARG
Solute carrier family 7, member 9/SLC7A9 (neutral AA)	604144	*****	2-BP DEL, 596TG	
Solute carrier family 7, member 9/SLC7A9 (neutral AA)	604144	*****	1-BP INS, 520T	
sterol-O-acyl transferase 1/SOAT1	102642	L21934	none found	
sterol-O-acyl transferase 2/SOAT2	601311	*****	none found	

Succinic semialdehyde dehydrogenase	271980	L34820	IVS9, G-T, +1	
Succinic semialdehyde dehydrogenase	271980	L34820	IVS5, G-A, +1	
SULFONYLUREA RECEPTOR 2	601439		none found	
Sulfotransferase, family 1C, member 3/SULT1C1	602385	U66036	none found	
Sulfotransferase, family 2B, member 1/SULT2B1	604125	NM_004605	none found	
Superoxide Dismutase 1/SOD1 (soluble)	147450	NM_000454		GLY37ARG
Superoxide Dismutase 1/SOD1 (soluble)	147450	NM_000454		LEU38VAL
Superoxide Dismutase 1/SOD1 (soluble)	147450	NM_000454		GLY41SER
Superoxide Dismutase 1/SOD1 (soluble)	147450	NM_000454		GLY41ASP
Superoxide Dismutase 1/SOD1 (soluble)	147450	NM_000454		HIS43ARG
Superoxide Dismutase 1/SOD1 (soluble)	147450	NM_000454		GLY85ARG
Superoxide Dismutase 1/SOD1 (soluble)	147450	NM_000454		GLY93CYS
Superoxide Dismutase 1/SOD1 (soluble)	147450	NM_000454		GLY93ALA
Superoxide Dismutase 1/SOD1 (soluble)	147450	NM_000454		GLU100GLY
Superoxide Dismutase 1/SOD1 (soluble)	147450	NM_000454		LEU106VAL

1/SOD1 (soluble)	147450	NM_00045 ⁴	ILE113THR
Superoxide Dismutase			
1/SOD1 (soluble)	147450	NM_00045 ⁴	ALA4VAL
Superoxide Dismutase			
1/SOD1 (soluble)	147450	NM_00045 ⁴	HIS46ARG
Superoxide Dismutase			
1/SOD1 (soluble)	147450	NM_00045 ⁴	ALA4THR
Superoxide Dismutase			
1/SOD1 (soluble)	147450	NM_00045 ⁴	ASP90ALA
Superoxide Dismutase			
1/SOD1 (soluble)	147450	NM_00045 ⁴	ILE104THE
Superoxide Dismutase			
1/SOD1 (soluble)	147450	NM_00045 ⁴	LEU144SER
Superoxide Dismutase			
1/SOD1 (soluble)	147450	NM_00045 ⁴	ALA145THR
Superoxide Dismutase			
1/SOD1 (soluble)	147450	NM_00045 ⁴	T-G, -10, 9-BP INS
Superoxide Dismutase			
1/SOD1 (soluble)	147450	NM_00045 ⁴	CYS6PHE
Superoxide Dismutase			
1/SOD1 (soluble)	147450	NM_00045 ⁴	THR151ILE
Superoxide Dismutase			
1/SOD1 (soluble)	147450	NM_00045 ⁴	GLU21LYS
Superoxide Dismutase			
1/SOD1 (soluble)	147450	NM_00045 ⁴	SER134ASN
Superoxide Dismutase			
1/SOD1 (soluble)	147450	NM_00045 ⁴	LEU84VAL
Superoxide Dismutase			
1/SOD1 (soluble)	147450	NM_00045 ⁴	GLY16SER
Superoxide Dismutase			
1/SOD1 (soluble)			

Superoxide Dismutase 1/SOD1 (soluble)	147450	NM_00045 ₄	LEU126TER
Superoxide Dismutase 1/SOD1 (soluble)	147450	NM_00045 ₄	VS4AS, A-G, -11
Superoxide Dismutase 1/SOD1 (soluble)	147450	NM_00045 ₄	GLY72SER
Superoxide Dismutase 1/SOD1 (soluble)	147450	NM_00045 ₄	Val7-->Glu
Superoxide Dismutase 2/SOD2 (mitochondrial)	147460	X65965	ALA16VAL
Superoxide Dismutase 3/SOD3 (extracellular)	185490	NM_00310 ₂	ARG213GLY
Superoxide Dismutase 3/SOD3 (extracellular)	185490	NM_00310 ₂	A24IG
Superoxide Dismutase 3/SOD3 (extracellular)	185490	NM_00310 ₂	C280T
Thiopurine methyltransferase (6- mercaptopurine detoxification)	187680	U12387	ALA80PRO
Thiopurine methyltransferase (6- mercaptopurine detoxification)	187680	U12387	ALA154THR
Thiopurine methyltransferase (6- mercaptopurine detoxification)	187680	U12387	TYR240CYS
Thiopurine methyltransferase (6- mercaptopurine detoxification)	187680	U12387	IVS9AS, G-A, -1

SD-144141.1

mercaptapurine detoxification)	187680	U12387	ALA154THR
Thiopurine methyltransferase (6- mercaptapurine detoxification)	187680	U12387	TYR240CYS
Thiopurine methyltransferase (6- mercaptapurine detoxification)	187680	U12387	ARG215HIS
Thiopurine methyltransferase (6- mercaptapurine detoxification)	187680	U12387	G460 to A
Thiopurine methyltransferase (6- mercaptapurine detoxification)	187680	U12387	A719 to G
Thiopurine methyltransferase (6- mercaptapurine detoxification)	187680	U12387	VNTR promoter
Thiopurine methyltransferase (6- mercaptapurine detoxification)	187680	U12387	G644A
Thiopurine methyltransferase (6- mercaptapurine detoxification)	187680	U12387	G238C

methytransferase (6- mercaptopurine detoxification) Thiopurine	187680	U12387	T681G	
methytransferase (6- mercaptopurine detoxification) Thiopurine	187680	U12387	C-->T at nucleotide - 178	
methytransferase (6- mercaptopurine detoxification) Thiopurine	187680	U12387	T-->G681	
methytransferase (6- mercaptopurine detoxification) TRANSCRIPTION FACTOR P65	164014	L19067		494, Glu-Asp
glycosyltransferase 1/UGT1	191740	NM_00107 2	13-BP DEL	
glycosyltransferase 1/UGT1	191740	NM_00107 2		SER-PHE
glycosyltransferase 1/UGT1	191740	NM_00107 2		GLN331TER
glycosyltransferase 1/UGT1	191740	NM_00107 2		ARG341TER
glycosyltransferase 1/UGT1	191740	NM_00107 2		GLN331ARG

1/UGT1	191740	NM_00107 2	PHE170DEL
UDP glycosyltransferase 1/UGT1			
UDP glycosyltransferase 1/UGT1	191740	NM_00107 2	SER376PHE
UDP glycosyltransferase 1/UGT1	191740	NM_00107 2	GLY309GLU
UDP glycosyltransferase 1/UGT1	191740	NM_00107 2	CYS-TER
UDP glycosyltransferase 1/UGT1	191740	NM_00107 2	PRO229GLN
UDP glycosyltransferase 1/UGT1	191740	NM_00107 2	2-BP INS, TA, TATAA ELEMENT
UDP glycosyltransferase 1/UGT1	191740	NM_00107 2	1-BP INS, 470T
UDP glycosyltransferase 1/UGT1	191740	NM_00107 2	IVS1, G-C, +1
UDP glycosyltransferase 1/UGT1	191740	NM_00107 2	145C-T
UDP glycosyltransferase 1/UGT1	191740	NM_00107 2	IVS3, A-G, -2

UDP glycosyltransferase 8/UGT8	601291	U30930	none found	
UDP glycosyltransferase family 2, member B10/UGT2B10	600070	NM_00107 5	none found	
UDP glycosyltransferase family 2, member B15/UGT2B15	600069	U06641		asp851yr
UDP glycosyltransferase family 2, member B17/UGT2B17	601903	NM_00107 7	none found	
UDP glycosyltransferase family 2, member B4/UGT2B4	600067	NM_00107 3		asp458glu
UDP glycosyltransferase family 2, member B4/UGT2B4	600067	NM_00107 3		leu109phe
UDP glycosyltransferase family 2, member B4/UGT2B4	600067	NM_00107 3		leu396phe
UDP glycosyltransferase family 2, member B7/UGT2B7	600068	NM_00107 4	none found	

UDP-glucuronosyltransferase ^e	218800	AJ005162	none found
Vesicular acetylcholine transporter	600336	NM_003055	none found
Vesicular Amine Transporter 1; VAT1	193002	*****	none found
Vesicular Amine Transporter 2; VAT2	193001	L09118	TaqI XX

Table 21. Identified Variances in Genes or Related Pathways involved in Inflammation and Immune Disease

3,5 cyclic nucleotide phosphodiesterase (HSPDE1A3A)	171890	U40370	none found
activated leucocyte cell adhesion molecule/CD6 ligand/ALCAM	601662	L38608	none found
alpha-2-macroglobulin	103950	M11313	VAL1000ILE
alpha-2-macroglobulin	103950	M11313	CYS972TYR
alpha-2-macroglobulin	103950	M11313	deletion of the intron
alpha-2-macroglobulin	103950	M11313	ARG681HIS
alpha-2-macroglobulin	103950	M11313	EX18DEL
alpha-2-macroglobulin	103950	M11313	5-BP DEL
alpha-2-macroglobulin	103950	M11313	intronic

alpha-2-macroglobulin	103950	M11313	polymorphism EcoRI	ILE333VAL
antigen peptide transporter 1/MHC 1/TAP1	170260	X57522		
antigen peptide transporter 1/MHC 1/TAP1	170260	X57522		ASP637GLY
antigen peptide transporter 1/MHC 1/TAP1	170260	X57522		ARG659GLN
antigen peptide transporter 1/MHC 1/TAP1	170260	X57522	518 (GTC-->ATC)	Val-->Ile
antigen peptide transporter 1/MHC 1/TAP1	170260	X57522	G-->T substitution in the promoter region	
antigen peptide transporter 1/MHC 1/TAP1	170260	X57522	10-bp insert in intron 9	
antigen peptide transporter 1/MHC 1/TAP1	170260	X57522	G-->T 80bp 3' of termination codon	
antigen peptide transporter 2/MHC 2/TAP2	170261	Z22935		Ala665Thr
antigen peptide transporter 2/MHC 2/TAP2	170261	Z22935		Gln687Stop
antigen peptide transporter 2/MHC 2/TAP2	170261	Z22935		ILE379VAL

2/TAP2	147678	X65019	none found
apoptosis-related			
cystein protease			
1/interleukin 1-beta			
converting			
enzyme/ICE/caspase			
1/CASP1			
beta-1-adrenergic	109630	J03019	C1165G ARG389GLY
receptor; Adrb1			
beta-1-adrenergic	109630	J03019	Bgl I.
receptor; Adrb1			
Beta-2-Adrenergic	109690	M15169	val 34 met
Receptor; Adrb2			
Beta-2-Adrenergic	109690	M15169	A-->G -1343
Receptor; Adrb2			
Beta-2-Adrenergic	109690	M15169	C-->G -468
Receptor; Adrb2			
Beta-2-Adrenergic	109690	M15169	G-->A -1023
Receptor; Adrb2			
Beta-2-Adrenergic	109690	M15169	G-->A -654
Receptor; Adrb2			
Beta-2-Adrenergic	109690	M15169	T-->A -1429
Receptor; Adrb2			
Beta-2-Adrenergic	109690	M15169	T-->C -367
Receptor; Adrb2			
Beta-2-Adrenergic	109690	M15169	Fnu4HI
Receptor; Adrb2			
Beta-2-Adrenergic	109690	M15169	T-->C -20
Receptor; Adrb2			
Beta-2-Adrenergic	109690	M15169	T-->C -47
Receptor; Adrb2			

Beta-3-Adrenergic Receptor; Adrb3	109691	X70811	TRP64ARG
Beta-3-Adrenergic Receptor; Adrb3	109691	X70811	intron 1 g1856t
Beta-Adrenergic Receptor Kinase 2; Adrbk2	109636	X69117	none found
bradykinin receptor B1/BDKRB1 G	600337	U12512	9-base pair deletion
protein-coupled bradykinin receptor B1/BDKRB1 G	600337	U12512	A1098-->G
protein-coupled bradykinin receptor B1/BDKRB1 G	600337	U12512	C181-->T
protein-coupled bradykinin receptor B1/BDKRB1 G	600337	U12512	G-699-->C
protein-coupled bradykinin receptor B2/BDKRB2 G	113503	X86164	-845C/T
protein-coupled bradykinin receptor B2/BDKRB2 G	113503	X86165	-704C/T
protein-coupled bradykinin receptor B2/BDKRB2 G	113503	X86166	-649insG
protein-coupled bradykinin receptor B2/BDKRB2 G	113503	X86167	-640T/C

bradykinin receptor B2/BDKKRB2 G	113503	X86168	-536C/T	
protein-coupled bradykinin receptor B2/BDKKRB2 G	113503	X86169	-412C/G	
protein-coupled bradykinin receptor B2/BDKKRB2 G	113503	X86170	-143C/T	
protein-coupled bradykinin receptor B2/BDKKRB2 G	113503	X86171	-78C/T	
protein-coupled bradykinin receptor B2/BDKKRB2 G	113503	X86172		T21M
protein-coupled bradykinin receptor B2/BDKKRB2 G	113503	X86173	9 bp de (-)21-29	
protein-coupled bradykinin receptor B2/BDKKRB2 G	113503	X86174	C>T promoter 54	
protein-coupled bradykinin receptor B2/BDKKRB2 G	113503	X86175	tandem repeat near promoter	
protein-coupled bradykinin receptor B2/BDKKRB2 G	113503	X86176		R14C
protein-coupled bradykinin receptor B2/BDKKRB2 G	113503	X86177	repeat 3'UTR	
protein-coupled Ca Channel alpha1a	601011	AF004884		ARG192GLN

(alt. splice) L-Type Ca Channel alpha	601011	AF004884	THR666MET
(alt. splice) L-Type Ca Channel alpha	601011	AF004884	VAL714ALA
(alt. splice) L-Type Ca Channel alpha	601011	AF004884	ILE1811LEU
(alt. splice) L-Type Ca Channel alpha	601011	AF004884	1-BP DEL, 4073C frameshift
(alt. splice) L-Type Ca Channel alpha	601011	AF004884	G-to-A first nucleotide of intron 24 (CAG) _n
Ca Channel alpha (alt. splice) L-Type	601011	AF004884	GLY293ARG
Ca Channel alpha (alt. splice) L-Type	601011	AF004884	ASP715GLU
Ca Channel alpha (alt. splice) L-Type	601011	AF004884	C4914T premature stop
Ca Channel gamma L-Type	114209	L07738	none found
Ca ²⁺ -dependent phospholipase A2	601192	U03090	none found
CD3E antigen, epsilon polypeptide (TiT3 complex)	186830	X03884	T-to-C splice change
CD3E antigen, epsilon polypeptide (TiT3 complex)	186830	X03884	TRP59TER
CD3E antigen, epsilon	186830	X03884	TaqI

polypeptide (TiT3 complex)	186740	X04145	MET1VAL
CD3G antigen, gamma polypeptide (TiT3 complex)	186740	X04145	17-BP DEL
CD3G antigen, gamma polypeptide (TiT3 complex)	186740	X04145	Mspl
Complement C1S component precursor (C1 esterase)	120580	J04080	4-BP DEL
Cyclooxygenase 1 COX1	176805	M59979	none found
Cyclooxygenase 2 COX2	600262	M90100	none found
H.sapiens ACTH-R gene for adrenocorticotrophic hormone receptor	None	X65633	none found
Histamine receptor H1	600167	AF026261	none found
Histamine receptor H2	142703	M64799	A649G
Histamine receptor H3	None	U31332	none found
Human DP prostanoide receptor (PTGDR) gene, 5 region and partial cds	600022	D38128	none found
Human IP gene for prostacyclin receptor,			

Human leukotriene-C4 synthase mRNA, complete cds	246530	U11552	promoter polymorphism
Human mRNA for prostacyclin synthase, complete cds	601699	D38145	none found
Human prostaglandin receptor ep1 subtype mRNA, complete cds	176802	L22647	none found
Intercellular adhesion molecule 1	147840	M24283	K/E 469
Intercellular adhesion molecule 1	147840	M24283	Dinucleotide repeat 3'
Intercellular adhesion molecule 2	146630	X15606	none found
Intercellular adhesion molecule 3	146631	X69819	LYS29MET
interferon-gamma receptor 2/IFNGR2	147569	U05875	Gln64Arg
interferon-gamma receptor 2/IFNGR2	147569		2-BP DEL, AG, NT278-279
interferon-gamma receptor 1/IFNGR1	107470	J03143	395C-A SER-TER
interferon-gamma receptor 1/IFNGR1	107470		1-BP DEL frameshift
interferon-gamma receptor 1/IFNGR1	107470		ILE87THR
interferon-gamma receptor 1/IFNGR1	107470		4-BP INS, 107TTAC
interferon-gamma	107470		G-A, +1

SD-144141.1

receptor 1/IFNGR1	107470	4-BP DEL, NT818	
interferon-gamma			
receptor 1/IFNGR1	107470		Val14Met
interferon-gamma			
receptor 1/IFNGR1	107470		TaqI
interferon-gamma			
receptor 1/IFNGR1	147720		TaqI
interleukin 1 beta			
(IL1b)			
interleukin 1 beta	147720	+5887 C --> T	
(IL1b)			
interleukin 1 beta	147720	exon 5 (position	
(IL1b)		+3953)	
interleukin 1 beta	147720	position -511	
(IL1b)			
interleukin 1 beta	147720		Asp106Asn
(IL1b)			
Interleukin 1 receptor	147679	86-bp tandem repeat	
antagonist			
Kallikrein Inhibitor	147935		
Kallikrein KLK1	147910	none found	
Kallikrein KLK1	147910	A1166-->C	
Kallikrein KLK2	147960	TaqI	
L-Type Ca Channel	114204	C to T at base 792	
alpha 2/delta		none found	
L-Type Ca Channel	114206		
alpha 1d		none found	
L-type voltage			
dependent calcium			
channel alpha 1C	114205	none found	
subunit/CACNA1C			

SD-144141.1

L-type voltage dependent calcium channel alpha 1S subunit/CACNA1S	114208	L33798	ARG1086HIS
L-type voltage dependent calcium channel alpha 1S subunit/CACNA1S	114208	L33798	ARG1239GLY
L-type voltage dependent calcium channel alpha 1S subunit/CACNA1S	114208	L33798	ARG1239HIS
L-type voltage dependent calcium channel alpha 1S subunit/CACNA1S	114208	L33798	ARG528HIS
Leukocyte integrin alpha-4	192975	L12002	none found
Leukocyte integrin alpha-d	602453	U40274	none found
Leukocyte integrin alpha-l	153370	Y00796	none found
Leukocyte integrin alpha-m	120980	J04145	none found
Leukocyte integrin alpha-x	151510	M81695	none found
Leukocyte integrin beta-1	135630	U28252	none found
Leukocyte integrin beta-2	600065	M15395	ARG593CYS
Leukocyte integrin	600065	M15395	LYS196THR

SD-144141.1

Leukocyte integrin beta-2	600065	M15395	LEU149PRO
Leukocyte integrin beta-2	600065	M15395	GLY169ARG
Leukocyte integrin beta-2	600065	M15395	ATG-to-AAG initiation codon
Leukocyte integrin beta-2	600065	M15395	ARG586TRP
Leukocyte integrin beta-2	600065	M15395	12-bp insertion pro-ser-ser-gln
Leukocyte integrin beta-2	600065	M15395	ASN351SER
Leukocyte integrin beta-2	600065	M15395	PRO178LEU
Leukocyte integrin beta-2	600065	M15395	ASP128ASN
Leukocyte integrin beta-2	600065	M15395	G-A, splice/donor site
Leukocyte integrin beta-2	600065	M15395	GLY284SER
Leukocyte integrin beta-2	600065	M15395	SER138PRO
Leukocyte integrin beta-2	600065	M15395	GLY273ARG
Leukocyte integrin beta-2	600065	M15395	S138P
Leukocyte integrin beta-2	173470	M35999	ARG214GLN
Leukocyte integrin beta-3	173470	M35999	ASP119TYR

SD-144141.1

Leukocyte integrin beta-3	173470	M35999	ARG214TRP
Leukocyte integrin beta-3	173470	M35999	SER752PRO
Leukocyte integrin beta-3	173470	M35999	ARG143GLN
Leukocyte integrin beta-3	173470	M35999	LEU33PRO
Leukocyte integrin beta-3	173470	M35999	PRO407ALA
Leukocyte integrin beta-3	173470	M35999	G-T, EXiDEL
Leukocyte integrin beta-3	173470	M35999	ARG489GLN
Leukocyte integrin beta-3	173470	M35999	CYS374TYR
Leukocyte integrin beta-3	173470	M35999	11.2-KB DEL
Leukocyte integrin beta-3	173470	M35999	ARG724TER
Leukocyte integrin beta-3	173470	M35999	GLU616TER
Leukocyte integrin beta-4	147557	X51841	1-BP INS, 3801T
Leukocyte integrin beta-4	147557	X51841	1-BP DEL, 1150G
Leukocyte integrin beta-4	147557	X51841	LEU156PRO
Leukocyte integrin beta-4	147557	X51841	ARG554TER
Leukocyte integrin beta-4	147557	X51841	CYS61TYR

SD-144141.1

beta-4 Leukocyte integrin	147557	X51841	CYS562ARG
beta-4 Leukocyte integrin	147557	X51841	IVS30DS, G-A, +1
beta-4 Leukocyte integrin	147557	X51841	TRP1478TER
beta-4 Leukocyte integrin	147557	X51841	CYS38ARG
beta-4 Leukocyte integrin	147557	X51841	1-BP DEL, 4776G
beta-4 Leukocyte integrin	147557	X51841	3434delT
beta-4 Leukocyte integrin	147557	X51841	8-bp deletion
beta-4 Leukocyte integrin	147559	M68892	none found
beta-7 Leukotriene A4 hydrolase	151570	J03459	none found
Leukotriene C4 receptor			none found
Leukotriene D4/E4 receptor			none found
lipocortin 1/annexin 1	151690	X05908	none found
lipocortin 2/annexin 2	151740	D00017	none found
lipocortin 3/annexin 3	106490	M20560	BglII
lipocortin 3/annexin 3	106490	M20560	SalI
lipocortin 3/annexin 3	106490	M20560	tandem repeat
Lipoxygenases: 12- lipoxygenase (platelet)	152391	M62982	TAAA none found

SD-144141.1

Lipoxygenases: 5-lipoxygenase (leukocytes)	152390	J03571	none found
lymphotoxin beta receptor (TNFR superfamily, member 3/LTBR)	600979	L04270	none found
N-acylamino acid aminohydrolase	104620	L07548	none found
P2Y7	601531	D89078	none found
purinoceptor/leukotriene B4 receptor/G protein-coupled			
Phospholipase A-2 (PLA-2) lung	172410	M21054	none found
Phospholipase C beta-3	600230	Z26649	none found
Phospholipase C delta-1	602142	U09117	none found
Phospholipase C epsilon	600597	D42108	none found
Phospholipase C gamma-1	172420	M34667	none found
Phospholipase C gamma-2	600220	M37238	none found
Phospholipase C, beta 4	600810	L41349	none found
Platelet-activating factor receptor	173393	M76674	none found
Prostaglandin 15-OH dehydrogenase (PGDH)	601688	J05594	none found

SD-144141.1

Prostaglandin E receptor 2 (subtype EP2), 53kD	601586	L28175	none found
Prostaglandin E receptor 3 (subtype EP3) {alternative products}	176806	X83861	none found
PROSTAGLANDIN E2 RECEPTOR, EP2 SUBTYPE	176804	U19487	none found
PROSTAGLANDIN F RECEPTOR	600563	L24470	none found
PROSTAGLANDIN F2 ALPHA RECEPTOR		U26664	none found
prostaglandin transporter hPGT	601460	U70867	none found
recombination activating gene 1/RAG1	179615	M29474	GLU722LYS
recombination activating gene 1/RAG1	179615	M29474	GLU774TER
recombination activating gene 1/RAG1	179615	M29474	TYR938TER
recombination activating gene 1/RAG1	179615	M29474	ALA156VAL
recombination activating gene	179615	M29474	ARG56IHIS

SD-144141.1

1/RAG1 recombination activating gene 1/RAG1	179615	M29474	ARG396CYS
recombination activating gene 1/RAG1	179615	M29474	TYR912CYS
recombination activating gene 1/RAG1	179615	M29474	ARG396HIS
recombination activating gene 1/RAG1	179615	M29474	ASP429GLY
recombination activating gene 1/RAG1	179615	M29474	ARG561CYS
recombination activating gene 1/RAG1	179615	M29474	ARG737HIS
recombination activating gene 1/RAG1	179615	M29474	13-BP DEL, NT1723
recombination activating gene 1/RAG1	179615	M29474	2-BP DEL, NT368
recombination activating gene 2/RAG2	179616		CYS476TYR
recombination activating gene 2/RAG2	179616		ARG220GLN

SD-144141.1

recombination activating gene 2/RAG2	179616	CYS41TRP	
recombination activating gene 2/RAG2	179616	MET285ARG	
regulator of G-protein signalling 1/RGS1	600323	X73427	none found
Retinoic acid receptor, alpha/RARA	180240	X06538	7-base deletion frameshift
Retinoic acid receptor, alpha/RARA	180240	X06538	Arg272Gln
Retinoic acid receptor, alpha/RARA	180240	X06538	Met297Leu
Retinoic acid receptor, alpha/RARA	180240	X06538	codon 411 C to T
Retinoic acid receptor, beta/RARB	180220	X07282	none found
Retinoic acid receptor, gamma/RARG	180190	M24857	none found
serotonin 5-HT receptors 5-HT3, gated ion channel	182139	D49394	none found
signaling lymphocytic activation molecule/SLAM	603492	U33017	none found
small inducible cytokine subfamily A (Cys-Cys), member 2/monocyte chemotactic protein	158105	M28226	-2518 (G or A)

SD-144141.1

1/MCP1/SCYA2 small inducible cytokine subfamily A (Cys-Cys), member 2/monocyte chemotactic protein	158105	M28226	-2076 (A or T)	
1/MCP1/SCYA2 small inducible cytokine subfamily A (Cys-Cys), member 3/macrophage inflammatory protein 1A/MIP1A/SCYA3	182283	M25315	none found	
Solute carrier family 4, anion exchanger, member 1 (MEDIATES EXCHANGE OF INORGANIC ANIONS ACROSS THE MEMBRANE)	109270	M27819		LYS56GLU
Solute carrier family 4, anion exchanger, member 1 (MEDIATES EXCHANGE OF INORGANIC ANIONS ACROSS THE MEMBRANE)	109270	M27819	24-BP DEL CODONS 400- 408	
Solute carrier family 4, anion exchanger,	109270	M27819		PRO327ARG

member 1 (MEDIATES EXCHANGE OF INORGANIC ANIONS ACROSS THE MEMBRANE) Solute carrier family 4, anion exchanger, member 1 (MEDIATES EXCHANGE OF INORGANIC ANIONS ACROSS THE MEMBRANE)	109270	M27819	GLU40LYS
Solute carrier family 4, anion exchanger, member 1 (MEDIATES EXCHANGE OF INORGANIC ANIONS ACROSS THE MEMBRANE)	109270	M27819	10-BP DUP
Solute carrier family 4, anion exchanger, member 1 (MEDIATES EXCHANGE OF INORGANIC ANIONS ACROSS THE MEMBRANE)	109270	M27819	GLU658LYS
Solute carrier family 4, anion exchanger, member 1 (MEDIATES EXCHANGE OF INORGANIC ANIONS ACROSS THE MEMBRANE)	109270	M27819	GLY771ASP

SD-144141.1

anion exchanger, member 1 (MEDIATES EXCHANGE OF INORGANIC ANIONS ACROSS THE MEMBRANE)	109270	M27819	GLN330TER
Solute carrier family 4, anion exchanger, member 1 (MEDIATES EXCHANGE OF INORGANIC ANIONS ACROSS THE MEMBRANE)	109270	M27819	ARG150TER
Solute carrier family 4, anion exchanger, member 1 (MEDIATES EXCHANGE OF INORGANIC ANIONS ACROSS THE MEMBRANE)	109270	M27819	89G-A

Solute carrier family 4, anion exchanger, member 1 (MEDIATES EXCHANGE OF INORGANIC ANIONS ACROSS THE MEMBRANE)	109270	M27819	VAL557MET
Solute carrier family 4, anion exchanger, member 1 (MEDIATES EXCHANGE OF INORGANIC ANIONS ACROSS THE MEMBRANE)	109270	M27819	ARG589HIS
Solute carrier family 4, anion exchanger, member 1 (MEDIATES EXCHANGE OF INORGANIC ANIONS ACROSS THE MEMBRANE)	109270	M27819	ARG589CYS
Solute carrier family 4, anion exchanger, member 1 (MEDIATES EXCHANGE OF INORGANIC ANIONS ACROSS THE MEMBRANE)	109270	M27819	SER613PHE

SD-144141.1

THE MEMBRANE) Solute carrier family 4, anion exchanger, member 1 (MEDIATES EXCHANGE OF INORGANIC ANIONS ACROSS THE MEMBRANE)	109270	M27819	ARG589SER
Solute carrier family 4, anion exchanger, member 1 (MEDIATES EXCHANGE OF INORGANIC ANIONS ACROSS THE MEMBRANE)	109270	M27819	GLY701ASP
Solute carrier family 4, anion exchanger, member 1 (MEDIATES EXCHANGE OF INORGANIC ANIONS ACROSS THE MEMBRANE)	109270	M27819	PRO854LEU
Solute carrier family 4, anion exchanger, member 1 (MEDIATES EXCHANGE OF INORGANIC ANIONS ACROSS THE MEMBRANE)	109270	M27819	GLY130ARG

ANIONS ACROSS THE MEMBRANE)	109270	M27819	THR837ALA
Solute carrier family 4, anion exchanger, member 1 (MEDIATES EXCHANGE OF INORGANIC ANIONS ACROSS THE MEMBRANE)	176947	L05148	GG-AG, -11
T cell receptor-associated protein tyrosine kinase ZAP-70/ZAP70	176947	L05148	G-A, -9
T cell receptor-associated protein tyrosine kinase ZAP-70/ZAP70	176947	L05148	SER518ARG
T cell receptor-associated protein tyrosine kinase ZAP-70/ZAP70	176947	L05148	13-BP DEL frameshift
Thromboxane A2 TP receptor, platelet and non-platelet	188070	U27325	ARG60LEU
Thromboxane synthase transforming growth	274180 190181	M80646 L11695	(CA)n intron 9 S387Y

factor, beta receptor I (activin A receptor type II-like kinase, 53kD)/TGFBRI	190182	M85079	2-BP INS frameshift	
transforming growth factor, beta receptor II (70-80kD)/TGFB2	190182	M85079	THR315MET	
transforming growth factor, beta receptor II (70-80kD)/TGFB2	190182	M85079	GG to TT Stop codon	
transforming growth factor, beta receptor II (70-80kD)/TGFB2	190182	M85079	a7g intron 2	
transforming growth factor, beta receptor II (70-80kD)/TGFB2	190182	M85079	a-4t intron 3	
transforming growth factor, beta receptor II (70-80kD)/TGFB2	190182	M85079	codon 128	
transforming growth factor, beta receptor II (70-80kD)/TGFB2	190182	M85079	ACA to GCA Thr to Ala	
transforming growth factor, beta receptor II (70-80kD)/TGFB2	190182	M85079	base in the polyadenine tract of exon 3 none found	
transforming growth factor, beta receptor III (betaglycan,	600742	L07594		

SD-144141.1

300kD)/TGFB β 3				
tumor necrosis factor alpha (TNFa)	191160	X01394	C-850T	
tumor necrosis factor alpha (TNFa)	191160	X01394	C-ins 5'UTR of exon 1	
tumor necrosis factor alpha (TNFa)	191160	X01394	G -238 A	
tumor necrosis factor alpha (TNFa)	191160	X01394	G -376 A	
tumor necrosis factor alpha (TNFa)	191160	X01394	-1,031 T-->C	
tumor necrosis factor alpha (TNFa)	191160	X01394	-863 C-->A	
tumor necrosis factor alpha (TNFa)	191160	X01394	-308 G/A	
tumor necrosis factor alpha (TNFa)	191160	X01394		ARG32TRP
tumor necrosis factor alpha (TNFa)	191160	X01394		LEU29SER
tumor necrosis factor alpha (TNFa)	191160	X01394	G-376A	
tumor necrosis factor alpha (TNFa)	191160	X01394	NcoI	
tumor necrosis factor alpha (TNFa)	191160	X01394	C to T, -857T	
TUMOR NECROSIS FACTOR RECEPTOR 1 PRECURSOR	191190	M58286		CYS333TYR
TUMOR NECROSIS FACTOR RECEPTOR 1 PRECURSOR	191190	M58286		THR50MET

SD-144141.1

TUMOR NECROSIS FACTOR RECEPTOR 1 PRECURSOR	191190	M58286	CYS30ARG
TUMOR NECROSIS FACTOR RECEPTOR 1 PRECURSOR	191190	M58286	CYS52PHE
TUMOR NECROSIS FACTOR RECEPTOR 1 PRECURSOR	191190	M58286	CYS88ARG
TUMOR NECROSIS FACTOR RECEPTOR 1 PRECURSOR	191190	M58286	CYS88TYR
Tumor necrosis factor receptor 2 (75kD)	191191	M32315	M196R
tumor necrosis factor type 1 receptor associated protein (TRAP1)	None	U12595	none found
tumor necrosis factor type 2 receptor associated protein (TRAP3)	601895	U12597	none found
Vascular cell adhesion molecule 1	192225	M60335	none found
vitamin D (1,25- dihydroxyvitamin D3) receptor/VDR	601769	J03258	GLY30ASP
vitamin D (1,25- dihydroxyvitamin D3) receptor/VDR	601769	J03258	ARG-GLY
vitamin D (1,25- dihydroxyvitamin D3) receptor/VDR	601769	J03258	TYR292TER

SD-144141.1

dihydroxyvitamin D3) receptor/VDR	601769	J03258	ARG77GLN
vitamin D (1,25- dihydroxyvitamin D3) receptor/VDR	601769	J03258	ARG47GLN
vitamin D (1,25- dihydroxyvitamin D3) receptor/VDR	601769	J03258	GLN149TER
vitamin D (1,25- dihydroxyvitamin D3) receptor/VDR	601769	J03258	ARG271LEU
vitamin D (1,25- dihydroxyvitamin D3) receptor/VDR	601769	J03258	GLY46ASP
vitamin D (1,25- dihydroxyvitamin D3) receptor/VDR	601769	J03258	HIS305GLN
vitamin D (1,25- dihydroxyvitamin D3) receptor/VDR	601769	J03258	ILE314SER
vitamin D (1,25- dihydroxyvitamin D3) receptor/VDR	601769	J03258	ARG391CYS
vitamin D (1,25- dihydroxyvitamin D3) receptor/VDR	601769	J03258	ARG30TER
vitamin D (1,25- dihydroxyvitamin D3)	601769	J03258	BsmI

receptor/VDR	601769	J03258	ATG to ACG initiation codon
vitamin D (1,25-dihydroxyvitamin D3) receptor/VDR	601769	J03258	Apa I
vitamin D (1,25-dihydroxyvitamin D3) receptor/VDR	601769	J03258	Taq I
vitamin D (1,25-dihydroxyvitamin D3) receptor/VDR	601769	J03258	codon 79 silent
vitamin D (1,25-dihydroxyvitamin D3) receptor/VDR	601769	J03258	base change in intron 3
vitamin D (1,25-dihydroxyvitamin D3) receptor/VDR	601769	J03258	EcoRV xx

Table 22. Identified Variances in Genes or Related Pathways involved in Endocrine and Metabolic Disease

2,3-cyclic nucleotide 3-phosphodiesterase	M19650	123830	none found
3beta hydroxysteroid dehydrogenase	M27137	109715	none found
a-glucosidase	Y00839	232300	EX18DEL

a-glucosidase	Y00839	232300	1-BP DEL	frameshift
a-glucosidase	Y00839	232300	T-G, -13 intron 1	
a-glucosidase	Y00839	232300		ARG725TRP
a-glucosidase	Y00839	232300		PRO545LEU
a-glucosidase	Y00839	232300		SER529VAL
a-glucosidase	Y00839	232300		GLY643ARG
a-glucosidase	Y00839	232300		GLU521LYS
a-glucosidase	Y00839	232300		GLU689LYS
a-glucosidase	Y00839	232300		ARG854TER
a-glucosidase	Y00839	232300		LEU299ARG
a-glucosidase	Y00839	232300		LYS903DEL
a-glucosidase	Y00839	232300		MET318THR
a-glucosidase	Y00839	232300		ASP91ASN
a-glucosidase	Y00839	232300		ASP645GLU
a-glucosidase AB	D42041	None	none found	
ACAT1	D90228	203750	1-BP INS, 1083A	
ACAT1	D90228	203750	1163 + 2	
ACAT1	D90228	203750	4-BP INS	
ACAT1	D90228	203750	828 + 1	
ACAT1	D90228	203750	IVS10, A-C, -2	
ACAT1	D90228	203750	IVS10, G-C, -1	
ACAT1	D90228	203750	IVS8, G-T, +1	
ACAT1	D90228	203750		ALA347THR
ACAT1	D90228	203750		GLY150ARG
ACAT1	D90228	203750		MET1LYS
ACAT1	D90228	203750		GLY379VAL
ACAT1	D90228	203750		GLN272TER
ACAT1	D90228	203750		GLU345DEL
ACAT1	D90228	203750		ASN93SER
ACAT1	D90228	203750		ILE312THR
ACAT1	D90228	203750		ALA333PRO

SD-144141.1

ACAT1	D90228	203750	1163 + 2 828 + 1 TaqI	N158D
ACAT2	S70154	100678		
ACAT2	S70154	100678		
ACAT2	S70154	100678		
ACAT2	S70154	100678	3804C-A	N158D Q272X
ACAT2	S70154	100678		
Adrenocorticotrophic hormone (ACTH)	M28636	176830		
Adrenocorticotrophic hormone (ACTH)	M28636	176830		
Adrenocorticotrophic hormone (ACTH)	M28636	176830	7133C DEL	
aldose reductase	M34720	103880		
Alpha Amylase 2A; pancreatic	M28443	104650		
androgen receptor	M20132	313700		
androgen receptor	M20132	313700	Hind III	silent Gln>Ter frameshift frameshift ala>thr glu629arg
androgen receptor	M20132	313700	(CAA)n	
androgen receptor	M20132	313700	(CAG)n	
androgen receptor	M20132	313700	(GGN)n	
androgen receptor	M20132	313700	5-KB DEL, EX F, G	
androgen receptor	M20132	313700	5-KB DEL, EX E	
androgen receptor	M20132	313700	C>T within exon B	
androgen receptor	M20132	313700	CAG340TAG	
androgen receptor	M20132	313700	Del T at 3286	
androgen receptor	M20132	313700	del1893	
androgen receptor	M20132	313700	G Codon 210 A	
androgen receptor	M20132	313700	G Codon 211 A	
androgen receptor	M20132	313700	G2314A	
androgen receptor	M20132	313700	G2677A	
androgen receptor	M20132	313700	HhaI	
androgen receptor	M20132	313700	HpaII	

androgen receptor	M20132	313700	Insert of 69 nucleotides MaeIII PARTIAL DEL Stu I	VAL730MET
androgen receptor	M20132	313700		ALA721THR
androgen receptor	M20132	313700		GLN902ARG
androgen receptor	M20132	313700		HIS874TYR
androgen receptor	M20132	313700		SER647ASN
androgen receptor	M20132	313700		THR877SER
androgen receptor	M20132	313700		ARG607GLN
androgen receptor	M20132	313700		VAL865LEU
androgen receptor	M20132	313700		VAL865MET
androgen receptor	M20132	313700		LYS588TER
androgen receptor	M20132	313700		CYS579PHE
androgen receptor	M20132	313700		PHE582TYR
androgen receptor	M20132	313700		pro892ser
androgen receptor	M20132	313700		PRO546SER
androgen receptor	M20132	313700		ILE869MET
androgen receptor	M20132	313700		GLU2LYS
androgen receptor	M20132	313700		ARG839CYS
androgen receptor	M20132	313700		ARG839HIS
androgen receptor	M20132	313700		GLN60TER
androgen receptor	M20132	313700		TRP794TER
androgen receptor	M20132	313700		LEU172TER
androgen receptor	M20132	313700		LEU707ARG
androgen receptor	M20132	313700		MET786VAL
androgen receptor	M20132	313700		TYR761CYS
androgen receptor	M20132	313700		ARG772CYS
androgen receptor	M20132	313700		598 or 599 ter

SD-144141.1

androgen receptor	M20132	313700	gly743val
androgen receptor	M20132	313700	Gln798Glu
androgen receptor	M20132	313700	arg726leu
androgen receptor	M20132	313700	LEU676PRO
androgen receptor	M20132	313700	ARG608LYS
androgen receptor	M20132	313700	val 581 phe
androgen receptor	M20132	313700	G214R
androgen receptor	M20132	313700	THR877ALA
androgen receptor	M20132	313700	Arg615His
androgen receptor	M20132	313700	Arg752Gln
androgen receptor	M20132	313700	arg840his
androgen receptor	M20132	313700	ALA771THR
androgen receptor	M20132	313700	LYS882TER
androgen receptor	M20132	313700	ARG846HIS
androgen receptor	M20132	313700	ARG773HIS
androgen receptor	M20132	313700	TRP717TER
androgen receptor	M20132	313700	ARG773CYS
androgen receptor	M20132	313700	VAL866MET
androgen receptor	M20132	313700	ARG855HIS
androgen receptor	M20132	313700	MET780ILE
Arginine Vasopressin Receptor 1A/AVPR1A	AF030625	600821	none found
Arginine Vasopressin Receptor 1B/AVPR1B	AF030512	600264	none found
Arginine vasopressin receptor 2	AF030626	304800	1-BP DEL
Arginine vasopressin receptor 2	AF030626	304800	1-BP DEL, 102G
Arginine vasopressin receptor 2	AF030626	304800	1-BP INS frameshift
Arginine vasopressin	AF030626	304800	1-BP INS 804 frameshift

SD-144141.1

receptor 2	AF030626	304800	15delC
Arginine vasopressin receptor 2			
receptor 2	AF030626	304800	28-bp del
Arginine vasopressin receptor 2			
Arginine vasopressin receptor 2	AF030626	304800	786delG frameshift
Arginine vasopressin receptor 2	AF030626	304800	CpG dinucleotides
Arginine vasopressin receptor 2	AF030626	304800	TYR280CYS
Arginine vasopressin receptor 2	AF030626	304800	P322H
Arginine vasopressin receptor 2	AF030626	304800	P322S
Arginine vasopressin receptor 2	AF030626	304800	ARG113TRP
Arginine vasopressin receptor 2	AF030626	304800	TRP71TER
Arginine vasopressin receptor 2	AF030626	304800	ALA132ASP
Arginine vasopressin receptor 2	AF030626	304800	ARG203CYS
Arginine vasopressin receptor 2	AF030626	304800	GLY185CYS
Arginine vasopressin receptor 2	AF030626	304800	TYR205CYS
Arginine vasopressin receptor 2	AF030626	304800	ASP85ASN
Arginine vasopressin receptor 2	AF030626	304800	GLY201ASP

Arginine vasopressin receptor 2	AF030626	304800	ARG337TER
Arginine vasopressin receptor 2	AF030626	304800	G107E
Arginine vasopressin receptor 2	AF030626	304800	L43P
Arginine vasopressin receptor 2	AF030626	304800	W193X
Arginine vasopressin receptor 2	AF030626	304800	ARG181CYS
Arginine vasopressin receptor 2	AF030626	304800	R137H
ATP-sensitive inwardly rectifying K-channel	U24660	600877	none found
Beta-3-Adrenergic Receptor; Adrb3	X70811	109691	intron 1 g1856t
Beta-3-Adrenergic Receptor; Adrb3	X70811	109691	TRP64ARG
BONE MORPHOGENETIC PROTEIN RECEPTOR, TYPE IB; BMPR1B		603248	none found
Calcitonin Receptor	U26553	114131	PRO463LEU
Calcitonin Receptor	U26553	114131	pro447leu
Calcitonin Related Peptide Receptor	U17473	114190	none found
Calcitonin Related Polypeptide Alpha	M26095	114130	1-BP INS, IVS4
Calcium-activated	U02632	600150	none found

SD-144141.1

potassium channel				
calpain, large	NM_000070	114240		ARG572GLN
polypeptide				
L3/CAPN3				
calpain, large	NM_000070	114240		ARG110TER
polypeptide				
L3/CAPN3				
calpain, large	NM_000070	114240		ARG769GLN
polypeptide				
L3/CAPN3				
calpain, large	NM_000070	114240		PRO319LEU
polypeptide				
L3/CAPN3				
calpain, large	NM_000070	114240		SER86PHE
polypeptide				
L3/CAPN3				
Carnitine	X78706	600184	none found	
Acetyltransferase				
Carnitine	D87812	600528		ASP454GLY
Palmitoyltransferase I				
(muscle)				
Carnitine	U09648	600650	413 delAG	
Palmitoyltransferase II				
Carnitine	U09648	600650		ARG631CYS
Palmitoyltransferase II				
Carnitine	U09648	600650		E174K
Palmitoyltransferase II				
Carnitine	U09648	600650		F352C
Palmitoyltransferase II				
Carnitine	U09648	600650		M647V
Palmitoyltransferase II				

SD-144141.1

Carnitine	U09648	600650	V368I
Palmitoyltransferase II			
Carnitine	U09648	600650	SER113LEU
Palmitoyltransferase II			
Carnitine	U09648	600650	R124Stop
Palmitoyltransferase II			
Carnitine	U09648	600650	ASP553ASN
Palmitoyltransferase II			
Carnitine	U09648	600650	PRO50HIS
Palmitoyltransferase II			
Carnitine	U09648	600650	GLU174LYS
Palmitoyltransferase II			
Carnitine	U09648	600650	PHE383TYR
Palmitoyltransferase II			
Carnitine	U09648	600650	F448L
Palmitoyltransferase II			
Carnitine	U09648	600650	G549D
Palmitoyltransferase II			
Carnitine	U09648	600650	ARG503CYS
Palmitoyltransferase II			
Carnitine	U09648	600650	TYR628SER
Palmitoyltransferase II			
CCAA T/ENHANCER- BINDING PROTEIN, GAMMA; CEBPG		138972	none found
Cell surface receptor for sulfonyleureas on pancreatic b cells	L78207	600509	EX35, G-A
Cell surface receptor for sulfonyleureas on pancreatic b cells	L78207	600509	G-A, -9 EXON ALPHA DEL

SD-144141.1

Cell surface receptor for sulfonyleureas on pancreatic b cells	L78207	600509	3-BP DEL	PHE1388DEL
Cell surface receptor for sulfonyleureas on pancreatic b cells	L78207	600509	ACC-->ACT	Thr759Thr
Cell surface receptor for sulfonyleureas on pancreatic b cells	L78207	600509	BRANCH POINT, A-G, -20	
Cell surface receptor for sulfonyleureas on pancreatic b cells	L78207	600509	Exon 16 -3c-->t	
Cell surface receptor for sulfonyleureas on pancreatic b cells	L78207	600509	G-A, -1	splice change
Cell surface receptor for sulfonyleureas on pancreatic b cells	L78207	600509	G-A, -1 exon 5	
Cell surface receptor for sulfonyleureas on pancreatic b cells	L78207	600509		ARG1353PRO
Cell surface receptor for sulfonyleureas on pancreatic b cells	L78207	600509		ARG1421CYS
Cell surface receptor for sulfonyleureas on pancreatic b cells	L78207	600509		ARG1494TRP
Cell surface receptor for sulfonyleureas on pancreatic b cells	L78207	600509		R275Q
Cell surface receptor for sulfonyleureas on pancreatic b cells	L78207	600509		V560M

for sulfonylureas on pancreatic b cells	L78207	600509	F591L
Cell surface receptor for sulfonylureas on pancreatic b cells	L78207	600509	G1382S
Cell surface receptor for sulfonylureas on pancreatic b cells	L78207	600509	H125Q
Cell surface receptor for sulfonylureas on pancreatic b cells	L78207	600509	N188S
Cell surface receptor for sulfonylureas on pancreatic b cells	L78207	600509	R1215Q
Cell surface receptor for sulfonylureas on pancreatic b cells	L78207	600509	R1394H
Cell surface receptor for sulfonylureas on pancreatic b cells	L78207	600509	T1139M
Cell surface receptor for sulfonylureas on pancreatic b cells	L78207	600509	S1370A
Cell surface receptor for sulfonylureas on pancreatic b cells	L78207	600509	GLY716VAL
cytochrome P450 aromatase (CYP19)	X13589	107910	(TTTA)n in intron 5

cytochrome P450 aromatase (CYP19)	X13589	107910	1-BP DEL, 408C	frameshift
cytochrome P450 aromatase (CYP19)	X13589	107910	G-->A at Val80	silent
cytochrome P450 aromatase (CYP19)	X13589	107910	G-1094 -A	ARG365GLN
cytochrome P450 aromatase (CYP19)	X13589	107910	G-to-A	Val370-to-Met
cytochrome P450 aromatase (CYP19)	X13589	107910	GT to AT exon and intron 3	
cytochrome P450 aromatase (CYP19)	X13589	107910	splice donor (GT>GC) of intron 6	29 extra amino acids ARG435CYS
cytochrome P450 aromatase (CYP19)	X13589	107910		CYS437TYR
cytochrome P450 aromatase (CYP19)	X13589	107910		Arg264cys
cytochrome P450 aromatase (CYP19)	X13589	107910		ARG375CYS
Cytochrome P450 reductase	S90469	124015	none found	
Cytochrome P450, subfamily IIB (phenobarbital- inducible), polypeptide 6	M29874	None	none found	
Cytochrome P450, subfamily XIA (cholesterol side chain cleavage)	M14565	118485	5' UTR pentanucleotide repeat	

SD-144141.1

SD-144141.1

Cytochrome P450, subfamily XVII (steroid 17-alpha-hydroxylase), adrenal hyperplasia	M14564	202110	1-BP DEL	frameshift
Cytochrome P450, subfamily XVII (steroid 17-alpha-hydroxylase), adrenal hyperplasia	M14564	202110	1-bp C del codon 131	
Cytochrome P450, subfamily XVII (steroid 17-alpha-hydroxylase), adrenal hyperplasia	M14564	202110	1-BP DEL	frameshift
Cytochrome P450, subfamily XVII (steroid 17-alpha-hydroxylase), adrenal hyperplasia	M14564	202110	4-BP DUP, EX8	
Cytochrome P450, subfamily XVII (steroid 17-alpha-hydroxylase), adrenal hyperplasia	M14564	202110	469-BP INS	
Cytochrome P450, subfamily XVII (steroid 17-alpha-hydroxylase), adrenal hyperplasia	M14564	202110	518-BP DEL	
Cytochrome P450, subfamily XVII (steroid 17-alpha-hydroxylase), adrenal hyperplasia	M14564	202110	7-BP DUP, EX2	

subfamily XVII (steroid 17-alpha- hydroxylase), adrenal hyperplasia	M14564	202110	IVS2, G-T, +5	
Cytochrome P450, subfamily XVII (steroid 17-alpha- hydroxylase), adrenal hyperplasia	M14564	202110	IVS7+5G to A	
Cytochrome P450, subfamily XVII (steroid 17-alpha- hydroxylase), adrenal hyperplasia	M14564	202110	T-->C promoter	
Cytochrome P450, subfamily XVII (steroid 17-alpha- hydroxylase), adrenal hyperplasia	M14564	202110		ARG347HIS
Cytochrome P450, subfamily XVII (steroid 17-alpha- hydroxylase), adrenal hyperplasia	M14564	202110		ARG358GLN
Cytochrome P450, subfamily XVII (steroid 17-alpha- hydroxylase), adrenal hyperplasia	M14564	202110		TRP17TER

(steroid 17-alpha-hydroxylase), adrenal hyperplasia	M14564	202110	PHE417CYS
Cytochrome P450, subfamily XVII (steroid 17-alpha-hydroxylase), adrenal hyperplasia	M14564	202110	PHE53/54 DEL
Cytochrome P450, subfamily XVII (steroid 17-alpha-hydroxylase), adrenal hyperplasia	M14564	202110	ARG239TER
Cytochrome P450, subfamily XVII (steroid 17-alpha-hydroxylase), adrenal hyperplasia	M14564	202110	PRO342THR
Cytochrome P450, subfamily XVII (steroid 17-alpha-hydroxylase), adrenal hyperplasia	M14564	202110	SER106PRO
Cytochrome P450, subfamily XVII (steroid 17-alpha-hydroxylase), adrenal hyperplasia	M14564	202110	PHE53DEL

SD-144141.1

hydroxylase), adrenal hyperplasia	M14564	202110	his373leu
Cytochrome P450, subfamily XVII (steroid 17-alpha- hydroxylase), adrenal hyperplasia	M14564	202110	Arg496Cys
Cytochrome P450, subfamily XVII (steroid 17-alpha- hydroxylase), adrenal hyperplasia	M14564	202110	Gln461Stop
Cytochrome P450, subfamily XVII (steroid 17-alpha- hydroxylase), adrenal hyperplasia	M14564	202110	ARG96TRP
Cytochrome P450, subfamily XVII (steroid 17-alpha- hydroxylase), adrenal hyperplasia	M14564	202110	none found
DOLICHOL- PHOSPHATE MANNOSYLTRANSF ERASE 1	603503		none found
DOLICHYL- PHOSPHATE MANNOSYLTRANSF ERASE 2 REGULATORY	603564		none found

SD-144141.1

SUBUNIT				
Endothelin Receptor Type A	D90348	131243	none found	
Endothelin Receptor Type B	L06623	131244	1-BP INS, 878T	
Endothelin Receptor Type B	L06623	131244		TRP275TER
Endothelin Receptor Type B	L06623	131244		ALA183GLY
Endothelin Receptor Type B	L06623	131244		TRP276CYS
Endothelin Receptor Type B	L06623	131244		SER305ASN
Endothelin Receptor Type B	L06623	131244		GLY57SER
estrogen receptor 1 (ESR1)	X03635	133430	RFLP (Pssl enzyme)	
estrogen receptor 1 (ESR1)	X03635	133430	RFLP (PvuII enzyme)	
Estrogen-preferring sulfotransferase/STE	NM_005420	600043	none found	
FATTY ACID COENZYME A LIGASE, LONG-CHAIN 2		152426	none found	
Folic Acid (Folate Receptor)	M28099	136430	none found	
follicle stimulating hormone-beta (FSH)	M16646	136530		CYS51GLY
follicle stimulating hormone-beta (FSH)	M16646	136530		FS87TER

SD-144141.1

FSH receptor	M65085	136435	566C-->T	ARG573CYS
FSH receptor	M65085	136435	BsmI	ILE160THR
FSH receptor	M65085	136435	HindIII	PHE591SER
FSH receptor	M65085	136435	PstI	Thr307Ala
FSH receptor	M65085	136435		Asp567Gly
FSH receptor	M65085	136435		Ser680Asn
FSH receptor	M65085	136435		Asp334Gly
FSH receptor	M65085	136435		ALA189VAL
G PROTEIN- COUPLED RECEPTOR 24; GPR24		601751	none found	
Glucagon	J04040	138030	Dinucleotide repeat	
glucagon receptor/GCGR	NM_0001 60	138033	Alu-repeat	
glucagon receptor/GCGR	NM_0001 60	138033		GLY40SER
glucagon-like peptide 1 receptor/GLP1R	U01156	138032	silent substitution in exon 6	
glucagon-like peptide 1 receptor/GLP1R	U01156	138032	simple tandem repeat DNA polymorphism none found	
glucagon-like peptide 2 receptor/GLP2R	*****	603659		
glucocorticoid receptor	M11050	138040	4-BP DEL	2 bases of the exon and the first 2

SD-144141.1

glucocorticoid receptor	M11050	138040	A to G 3'-splice junction of intron G	nucleotides of intron 6 frameshift
glucocorticoid receptor	M11050	138040	Base-pair deletion in exon 9	32 amino acid deletion
glucocorticoid receptor	M11050	138040	BcII	
glucocorticoid receptor	M11050	138040	T insertion 1188 and 1189	frameshift
glucocorticoid receptor	M11050	138040	trinucleotide insertion	Arg453
glucocorticoid receptor	M11050	138040	TthIII	
glucocorticoid receptor	M11050	138040		LEU753PHE
glucocorticoid receptor	M11050	138040		CYS736SER
glucocorticoid receptor	M11050	138040		CYS736THR
glucocorticoid receptor	M11050	138040		ILE747THR
glucocorticoid receptor	M11050	138040		ASP641VAL
glucocorticoid receptor	M11050	138040		L753F
glucocorticoid receptor	M11050	138040		Q710X
glucocorticoid receptor	M11050	138040		ASN363SER
glucocorticoid receptor	U25029	138040	none found	
glucocorticoid receptor	X03348	138040	none found	
GLUCOCORTICOID RECEPTOR- INTERACTING PROTEIN 1	601993	601993	none found	
glycogen synthase [human, liver, mRNA, 2912 nt]	S70004	138571	IVS6, G-C, +1	

glycogen synthase [human, liver, mRNA, 2912 nt]	S70004	138571	ALA339PRO
glycogen synthase [human, liver, mRNA, 2912 nt]	S70004	138571	ARG246TER
glycogen synthase [human, liver, mRNA, 2912 nt]	S70004	138571	ASN39SER
glycogen synthase [human, liver, mRNA, 2912 nt]	S70004	138571	HIS446ASP
glycogen synthase [human, liver, mRNA, 2912 nt]	S70004	138571	MET491ARG
glycogen synthase [human, liver, mRNA, 2912 nt]	S70004	138571	SER483PRO
glycogen synthase [human, liver, mRNA, 2912 nt]	S70004	138571	PRO479GLN
gonadotropin releasing hormone receptor/G protein- coupled/LHRHR/GNR HR	NM_0004 06	138850	ARG262GLN
gonadotropin releasing hormone receptor/G protein- coupled/LHRHR/GNR HR	NM_0004 06	138850	GLN106ARG

SD-144141.1

gonadotropin releasing hormone receptor/G protein-coupled/LHRHR/GNRHR	NM_000406	138850	TYR284CYS
gonadotropin releasing hormone receptor/G protein-coupled/LHRHR/GNRHR	NM_000406	138850	Mae III
Gonadotropin-releasing hormone (leutinizing-releasing hormone)	M12578	152760	none found
GROWTH FACTOR RECEPTOR-BOUND PROTEIN 2; GRB2		108355	none found
Growth hormone 1	V00519	139250	G-T, +1 intron 4
Growth hormone 1	V00519	139250	1-BP DEL, 371C
Growth hormone 1	V00519	139250	18-BP DEL, +28-45 intron 3
Growth hormone 1	V00519	139250	FS132TER
Growth hormone 1	V00519	139250	2-BP DEL
Growth hormone 1	V00519	139250	6.7-KB DEL
Growth hormone 1	V00519	139250	BglII
Growth hormone 1	V00519	139250	G-A, +1 intron 3
Growth hormone 1	V00519	139250	G-A, +28
Growth hormone 1	V00519	139250	G-C, +1 intron 3
Growth hormone 1	V00519	139250	G-C, +1 intron 4
Growth hormone 1	V00519	139250	HincII
Growth hormone 1	V00519	139250	MspI
Growth hormone 1	V00519	139250	T-C, +6 intron 3
Growth hormone 1	V00519	139250	ARG77CYS

Growth hormone 1	V00519	139250	ASP112GLY
Growth hormone 1	V00519	139250	TRP20TER
Growth hormone receptor	X06562	600946	none found
growth hormone releasing hormone receptor/G protein-coupled/GHRHR	U34195	139191	IVS8DS, G-C, -1 alternative splice
growth hormone releasing hormone receptor/G protein-coupled/GHRHR	U34195	139191	1-BP DEL frameshift
growth hormone releasing hormone receptor/G protein-coupled/GHRHR	U34195	139191	2-BP DEL frameshift
growth hormone releasing hormone receptor/G protein-coupled/GHRHR	U34195	139191	C to T codon 236. silent
growth hormone releasing hormone receptor/G protein-coupled/GHRHR	U34195	139191	EX4,6DEL
growth hormone releasing hormone receptor/G protein-coupled/GHRHR	U34195	139191	GAA180GAG silent
growth hormone releasing hormone receptor/G protein-coupled/GHRHR	U34195	139191	IVS4DS, G-A, +1 alternative splice

SD-144141.1

coupled/GHRHR growth hormone releasing hormone receptor/G protein- coupled/GHRHR	U34195	139191	IVS6AS, G-T, -1
growth hormone releasing hormone receptor/G protein- coupled/GHRHR	U34195	139191	IVS8AS, G-C, -1
growth hormone releasing hormone receptor/G protein- coupled/GHRHR	U34195	139191	IVS9DS, G-A, +1 frameshift
growth hormone releasing hormone receptor/G protein- coupled/GHRHR	U34195	139191	ARG161CYS
growth hormone releasing hormone receptor/G protein- coupled/GHRHR	U34195	139191	GLU224ASP
growth hormone releasing hormone receptor/G protein- coupled/GHRHR	U34195	139191	GLU44LYS
growth hormone releasing hormone receptor/G protein- coupled/GHRHR	U34195	139191	PHE96SER
growth hormone releasing hormone receptor/G protein- coupled/GHRHR	U34195	139191	ASP152HIS

SD-144141.1

receptor/G protein-coupled/GHRHR growth hormone releasing hormone	U34195	139191	GLN154PRO
receptor/G protein-coupled/GHRHR growth hormone releasing hormone	U34195	139191	ILE153THR
receptor/G protein-coupled/GHRHR growth hormone releasing hormone	U34195	139191	VAL155GLY
receptor/G protein-coupled/GHRHR growth hormone releasing hormone	U34195	139191	VAL144ILE
receptor/G protein-coupled/GHRHR growth hormone releasing hormone	U34195	139191	PRO131GLN
receptor/G protein-coupled/GHRHR growth hormone releasing hormone	U34195	139191	GLU224TER
receptor/G protein-coupled/GHRHR growth hormone releasing hormone	U34195	139191	P561T
receptor/G protein-coupled/GHRHR growth hormone	U34195	139191	ARG217TER

releasing hormone receptor/G protein- coupled/GHRHR	U34195	139191	ARG43TER
growth hormone releasing hormone receptor/G protein- coupled/GHRHR	U34195	139191	CYS38TER
growth hormone- releasing factor (GRF)	L29177		none found
Guanylate cyclase 1, soluble, alpha 2	X63282	601244	none found
Guanylate cyclase soluble, alpha-3 chain	X66534	139396	none found
Guanylate cyclase soluble, beta-1 chain	X66533	139397	none found
H.sapiens ACTH-R gene for adrenocorticotrophic hormone receptor	X65633	202200	C818A
H.sapiens ACTH-R gene for adrenocorticotrophic hormone receptor	X65633	202200	Ser74Ile
H.sapiens ALK-3 mRNA	Z22535	601299	none found
H.sapiens encoding PC1/PC3	X64810	162150	IVS5DS, A-C, +4

SD-144141.1

H.sapiens encoding PC1/PC3	X64810	162150	GLY483ARG
H.sapiens HNF4 mRNA for hepatocyte nuclear factor 4	X76930	600281	1-BP DEL PHE75T
H.sapiens HNF4 mRNA for hepatocyte nuclear factor 4	X76930	600281	GLN268TER
H.sapiens HNF4 mRNA for hepatocyte nuclear factor 4	X76930	600281	ARG154TER
H.sapiens HNF4 mRNA for hepatocyte nuclear factor 4	X76930	600281	ARG127TRP
H.sapiens HNF4 mRNA for hepatocyte nuclear factor 4	X76930	600281	VAL393ILE
H.sapiens HNF4 mRNA for hepatocyte nuclear factor 4	X76930	600281	Val/Met255
H.sapiens IL-1R2 mRNA for type II interleukin-1 receptor, (cell line CB23)	X59770	147811	none found
H.sapiens mRNA for beta subunit of epithelial amiloride- sensitive sodium channel	X87159	600760	1-BP INS, 592C
H.sapiens mRNA for beta subunit of	X87159	600760	32-BP DEL

SD-144141.1

epithelial amiloride-sensitive sodium channel	X87159	600760		ARG564TER
H.sapiens mRNA for beta subunit of epithelial amiloride-sensitive sodium channel	X87159	600760		PRO616LEU
H.sapiens mRNA for beta subunit of epithelial amiloride-sensitive sodium channel	X87159	600760		GLY37SER
H.sapiens mRNA for beta subunit of epithelial amiloride-sensitive sodium channel	X87159	600760		TYR618HIS
H.sapiens mRNA for beta subunit of epithelial amiloride-sensitive sodium channel	X87159	600760		PRO615SER
H.sapiens mRNA for carnitine carrier	Y10319	212138	I-BP INS	frameshift
H.sapiens mRNA for	Y10319	212138	110-BP DEL	

carnitine carrier					
H.sapiens mRNA for carnitine carrier	Y10319	212138	128-BP DEL		
H.sapiens mRNA for carnitine carrier	Y10319	212138			ARG166TER
H.sapiens mRNA for carnitine carrier	X82153	601105			TER330TRP
H.sapiens mRNA for cathepsin O	X82153	601105			GLY146ARG
H.sapiens mRNA for cathepsin O	X82153	601105			ARG241TER
H.sapiens mRNA for cathepsin O	X82153	601105			ALA277VAL
H.sapiens mRNA for cathepsin-O	X77383	600550	none found		
H.sapiens mRNA for CCAAT/enhancer binding protein alpha	Y11525	116897	none found		
H.sapiens mRNA for cyclic nucleotide phosphodiesterase	X95520	602047	1389 (A/G)		
H.sapiens mRNA for cyclic nucleotide phosphodiesterase	X95520	602047	dinucleotide repeat introns 12		
H.sapiens mRNA for cyclic nucleotide phosphodiesterase	X95520	602047	dinucleotide repeat introns 5		
H.sapiens mRNA for gamma subunit of epithelial amiloride- sensitive sodium	X87160	600761	none found		

SD-144141.1

channel				
H.sapiens mRNA for GlcNac-1-P transferase	Z82022	191350		none found
H.sapiens mRNA for glucose-dependant insulinotropic polypeptide receptor gene	X81832	147940		539G del
H.sapiens mRNA for glucose-dependant insulinotropic polypeptide receptor gene	X81832	147940		A-230C
H.sapiens mRNA for growth factor receptor tyrosine kinase	X61656	191306		none found
H.sapiens mRNA for microsomal triglyceride transfer protein	X75500	157147		-164 T->C
H.sapiens mRNA for microsomal triglyceride transfer protein	X75500	157147		-400 A-->T
H.sapiens mRNA for microsomal triglyceride transfer protein	X75500	157147		-493T/G
H.sapiens mRNA for microsomal triglyceride transfer	X75500	157147		1-BP DEL, 215C

SD-144141.1

protein H.sapiens mRNA for microsomal triglyceride transfer protein	X75500	157147	IVS, G-A, +5	
H.sapiens mRNA for microsomal triglyceride transfer protein	X75500	157147	IVS9AS, G-A, -1	
H.sapiens mRNA for microsomal triglyceride transfer protein	X75500	157147		ARG215TER
H.sapiens mRNA for parathyroid hormone receptor	X68596	168468	33-BP DEL	
H.sapiens mRNA for parathyroid hormone receptor	X68596	168468		HIS223ARG
H.sapiens mRNA for parathyroid hormone receptor	X68596	168468		THR410PRO
H.sapiens mRNA for parathyroid hormone receptor	X68596	168468		ARG383GLN
H.sapiens mRNA for parathyroid hormone receptor	X68596	168468		PRO132LEU
H.sapiens mRNA for phosphoenolpyruvate carboxykinase	X92720	261650	none found	

SD-144141.1

H.sapiens oculorhombin (aniridia) mRNA, complete cds	M77844	106210	IVS12DS, G-C, -1	
H.sapiens oculorhombin (aniridia) mRNA, complete cds	M77844	106210	2-BP INS	
H.sapiens oculorhombin (aniridia) mRNA, complete cds	M77844	106210	dinucleotide repeat promoter	
H.sapiens oculorhombin (aniridia) mRNA, complete cds	M77844	106210	EXON G DEL	
H.sapiens oculorhombin (aniridia) mRNA, complete cds	M77844	106210	IVS10AS, A-T, -2	
H.sapiens oculorhombin (aniridia) mRNA, complete cds	M77844	106210	IVS11DS, A-G, -2	
H.sapiens oculorhombin (aniridia) mRNA, complete cds	M77844	106210		ARG103TER
H.sapiens oculorhombin (aniridia) mRNA, complete cds	M77844	106210		SER353TER

SD-144141.1

complete cds H.sapiens oculorhombin (aniridia) mRNA, complete cds	M77844	106210	ARG26GLY
H.sapiens oculorhombin (aniridia) mRNA, complete cds	M77844	106210	I29V
H.sapiens oculorhombin (aniridia) mRNA, complete cds	M77844	106210	N17S
H.sapiens oculorhombin (aniridia) mRNA, complete cds	M77844	106210	Q178H
H.sapiens oculorhombin (aniridia) mRNA, complete cds	M77844	106210	R44Q
H.sapiens oculorhombin (aniridia) mRNA, complete cds	M77844	106210	Q422R
H.sapiens oculorhombin (aniridia) mRNA, complete cds	M77844	106210	ARG203TER
H.sapiens oculorhombin (aniridia) mRNA, complete cds	M77844	106210	ARG240TER

(aniridia) mRNA, complete cds H.sapiens oculorhombin	M77844	106210	GLY64VAL
(aniridia) mRNA, complete cds H.sapiens oculorhombin	M77844	106210	VAL126ASP
(aniridia) mRNA, complete cds H.sapiens oculorhombin	M77844	106210	GLN116TER
(aniridia) mRNA, complete cds H.sapiens oculorhombin	M77844	106210	I87R
(aniridia) mRNA, complete cds H.sapiens oculorhombin	M77844	106210	ARG125CYS
(aniridia) mRNA, complete cds H.sapiens oculorhombin	M77844	106210	VAL54ASP
H.sapiens PPP1R3 mRNA for protein phosphatase 1, glycogen-binding regulatory subunit	X78578	600917	5-BP INS/DEL 3'UTR

H.sapiens PPP1R3 mRNA for protein phosphatase 1, glycogen-binding regulatory subunit HEPATOCYTE NUCLEAR FACTOR 3-BETA; HNF3B HEPATOCYTE NUCLEAR FACTOR 3-GAMMA; HNF3G HEPATOCYTE NUCLEAR FACTOR	X78578	600917	ASP905TYR
		600288	none found
		602295	none found
		604164	none found
		600234	none found
		142940	none found
HMG CoA synthase (HSH1) mitochondrial HMG CoA synthase soluble	U12789 X66435	600234 142940	none found none found
HMGCoA reductase/HMGCR	NM_0008 59	142910	HgiAI
HMGCoA reductase/HMGCR	NM_0008 59	142910	ScrFI polymorphism in the 2nd intron
Homo sapiens (clone lamda-hPEC-3) phosphoenolpyruvate carboxykinase (PCK1) mRNA, complete cds Homo sapiens (clone PEBP2aA1) core- binding factor, runt domain, alpha subunit	L05144 L40992	261680 600211	none found 16-BP INS

SD-144141.1

1 (CBFA1) mRNA, 3' end of cds	L40992	600211	ALA REPEAT	
Homo sapiens (clone PEBP2aA1) core-binding factor, runt domain, alpha subunit 1 (CBFA1) mRNA, 3' end of cds	L40992	600211		MET175ARG
Homo sapiens (clone PEBP2aA1) core-binding factor, runt domain, alpha subunit 1 (CBFA1) mRNA, 3' end of cds	L40992	600211		SER191ASN
Homo sapiens (clone PEBP2aA1) core-binding factor, runt domain, alpha subunit 1 (CBFA1) mRNA, 3' end of cds	L40992	600211		TRP283TER
Homo sapiens acyl-CoA synthetase 4 (ACS4) mRNA, complete cds	AF030555	300157	none found	
Homo sapiens low	M28219	143890	ATn	

SD-144141.1

density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	EX2-6DEL
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	-19(CGG)n
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	1-BP DEL, 197G
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	1061-8T-->C
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	1650delG frameshift

receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	165delG
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	18-BP DUP
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	1846-1G-->A
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	2-BP DEL, 694AC
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	2199delCA

SD-144141.1

causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	2201delCA	
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	313 + 1G-->A	
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	335del10	frameshift
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	347delGCC	
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	4-BP INS, EX8	frameshift

hypercholesterolemia) mRNA, 3 end	M28219	143890	7-BP DEL	frameshift
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	785insG	
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	9-BP DEL	
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	AGG450AGA	silent
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	C766T	

mRNA, 3 end Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	EX13-14DEL
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	EX13-15DEL
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	EX13-15DUP
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	EX15DEL
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	EX16-17DEL

Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	EX16-18DEL
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	EX16DEL
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	EX17-18DEL
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	EX17DEL
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	EX2-12DEL
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	EX2-3DEL

density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	EX2-5DUP
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	EX2-8DUP
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	EX3-8DEL
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	EX4-6DEL
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	EX5DEL

SD-144141.1

receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	EX7-14DEL
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	EX7-8DEL
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	EX7DEL
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	EX9-10DEL
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	EX9DUP

SD-144141.1

causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	HhaI intron 9
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	HincII
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	IVS3, G-A, +1
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	IVS4, T-C, +2
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	null allele

hypercholesterolemia) mRNA, 3 end	M28219	143890	PvuII	
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	StuI	
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	T --> A28	
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890		ALA410THR
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890		VAL502MET

SD-144141.1

mRNA, 3 end Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	ASP283ASN
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	GLY27DEL
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	GLU207LYS
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	D154N
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	D206E

Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	V408M
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	GLY197DEL
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	C127W
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	C139G
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	E397X
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	GLN12TER

SD-144141.1

density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	GLY525ASP
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	GLY528ASP
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	CYS163TYR
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	ASP206GLU
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	CYS646TYR

SD-144141.1

receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	TRP66GLY
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	SER156LEU
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	GLY544VAL
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	R329X
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	ASN543HIS

causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	ASPI54ASN
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	N543H
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	Glu119-Lys
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	C152R
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	T705I

hypercholesterolemia) mRNA, 3 end	M28219	143890	Cys297-->Phe
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	asp147his
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	Trp469Stop
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	ASP412HIS
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	PRO664LEU

mRNA, 3 end Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	Ala370-->Thr
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	C356-->Y
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	CYS240PHE
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	Asp200-->Gly
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	C122X

Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	Pro84-->Ser
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	pro664leu
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	Cys646-->Tyr
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	Glu207-->Lys
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	Trp66-->Gly
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	CYS660TER

SD-144141.1

density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	TYR807CYS
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	TRP792TER
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	CYS210TER
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	GLY823ASP
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	LEU380HIS

receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	TYR167TER
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	VAL408MET
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	C331C
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	E119K
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	N494 N

SD-144141.1

causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	T383P
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	T705I
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	W23X
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	W556S
Homo sapiens low density lipoprotein receptor (FH 10 mutant causing familial hypercholesterolemia) mRNA, 3 end	M28219	143890	W66G

hypercholesterolemia) mRNA, 3 end	D89053	602371	none found
Homo sapiens mRNA for Acyl-CoA synthetase 3, complete cds			
Homo sapiens mRNA for estrogen receptor beta, complete cds	AB006590	601663	none found
Homo sapiens mRNA for perilipin, complete cds	AB005293	170290	none found
Homo sapiens mRNA for transient receptor potential protein TRP6	AJ006276	603652	none found
Homo sapiens mRNA for very-long-chain acyl-CoA synthetase, complete cds	D88308	603247	none found
Homo sapiens muscle glycogen phosphorylase (PYGM) mRNA, complete cds	AF066859	232600	IVS14, G-A, +1, 67- BP DEL
Homo sapiens muscle glycogen phosphorylase (PYGM) mRNA, complete cds	AF066859	232600	ARG49TER
Homo sapiens muscle glycogen	AF066859	232600	GLY204SER

phosphorylase (PYGM) mRNA, complete cds	AF066859	232600	LYS542THR
Homo sapiens muscle glycogen phosphorylase (PYGM) mRNA, complete cds			
Homo sapiens muscle glycogen phosphorylase (PYGM) mRNA, complete cds	AF066859	232600	METIGLY
Homo sapiens muscle glycogen phosphorylase (PYGM) mRNA, complete cds			
Homo sapiens muscle glycogen phosphorylase (PYGM) mRNA, complete cds	AF066859	232600	GLU654LYS
Homo sapiens muscle glycogen phosphorylase (PYGM) mRNA, complete cds			
Homo sapiens muscle glycogen phosphorylase (PYGM) mRNA, complete cds	AF066859	232600	LEU396PRO
Homo sapiens muscle glycogen phosphorylase (PYGM) mRNA, complete cds			
Homo sapiens muscle glycogen phosphorylase (PYGM) mRNA, complete cds	AF066859	232600	GLY685ARG
Homo sapiens muscle glycogen phosphorylase (PYGM) mRNA, complete cds			
Homo sapiens muscle glycogen phosphorylase (PYGM) mRNA, complete cds	AF066859	232600	ARG575TER

SD-144141.1

(PYGM) mRNA, complete cds Homo sapiens muscle glycogen phosphorylase (PYGM) mRNA, complete cds	AF066859	232600	GLN665GLU
Homo sapiens muscle glycogen phosphorylase (PYGM) mRNA, complete cds	AF066859	232600	LYS753, DEL A
Homo sapiens muscle glycogen phosphorylase (PYGM) mRNA, complete cds	AF066859	232600	METVAL
Homo sapiens muscle glycogen phosphorylase (PYGM) mRNA, complete cds	AF066859	232600	GLU540TER
Homo sapiens somatostatin receptor (SSTR4) gene, complete cds	L07833	182454	none found
Homo sapiens sorbitol dehydrogenase gene, complete cds	U07361	182500	none found
HOMOLOG OF SONIC HEDGEHOG		600725	GLY31ARG

SD-144141.1

HOMOLOG OF SONIC HEDGEHOG	600725	GLN100TER
HOMOLOG OF SONIC HEDGEHOG	600725	LYS105TER
HOMOLOG OF SONIC HEDGEHOG	600725	TRP117GLY
HOMOLOG OF SONIC HEDGEHOG	600725	TRP117ARG
Human (HepG2) glucose transporter gene mRNA, complete cds	K03195 138140	GCT15GCC silent
Human (HepG2) glucose transporter gene mRNA, complete cds	K03195 138140	XbaI
Human (HepG2) glucose transporter gene mRNA, complete cds	K03195 138140	DEL
Human (HepG2) glucose transporter gene mRNA, complete cds	K03195 138140	LYS456TER
Human (HepG2) glucose transporter gene mRNA, complete cds	K03195 138140	TYR449TER
Human activin receptor-like kinase (ALK-5) mRNA,	L11695 190181	S387Y

complete cds				
Human bek mRNA for fibroblast growth factor receptor-BEK	X52832	176943	ALU INS	
Human bek mRNA for fibroblast growth factor receptor-BEK	X52832	176943		CYS342TYR
Human bek mRNA for fibroblast growth factor receptor-BEK	X52832	176943		CYS342ARG
Human bek mRNA for fibroblast growth factor receptor-BEK	X52832	176943		CYS342SER
Human bek mRNA for fibroblast growth factor receptor-BEK	X52832	176943		TYR340HIS
Human bek mRNA for fibroblast growth factor receptor-BEK	X52832	176943		SER354CYS
Human bek mRNA for fibroblast growth factor receptor-BEK	X52832	176943		ALA344ALA
Human bek mRNA for fibroblast growth factor receptor-BEK	X52832	176943		ALA344GLY
Human bek mRNA for fibroblast growth factor receptor-BEK	X52832	176943		TYR328CYS
Human bek mRNA for fibroblast growth factor receptor-BEK	X52832	176943		SER347CYS

SD-144141.1

Human bek mRNA for fibroblast growth factor receptor-BEK	X52832	176943	SER252TRP
Human bek mRNA for fibroblast growth factor receptor-BEK	X52832	176943	PRO253ARG
Human bek mRNA for fibroblast growth factor receptor-BEK	X52832	176943	THR341PRO
Human bek mRNA for fibroblast growth factor receptor-BEK	X52832	176943	CYS342TRP
Human bek mRNA for fibroblast growth factor receptor-BEK	X52832	176943	GLN289PRO
Human bek mRNA for fibroblast growth factor receptor-BEK	X52832	176943	TYR375CYS
Human bek mRNA for fibroblast growth factor receptor-BEK	X52832	176943	SER372CYS
Human bek mRNA for fibroblast growth factor receptor-BEK	X52832	176943	SER252PHE
Human bek mRNA for fibroblast growth factor receptor-BEK	X52832	176943	PRO253SER
Human bek mRNA for fibroblast growth factor receptor-BEK	X52832	176943	TRP290CYS
Human bek mRNA for fibroblast growth factor receptor-BEK	X52832	176943	LYS292GLU

SD-144141.1

fibroblast growth factor receptor-BEK	X52832	176943	TRP290ARG
Human bek mRNA for fibroblast growth factor receptor-BEK	X52832	176943	TRP290GLY
Human bek mRNA for fibroblast growth factor receptor-BEK	X52832	176943	LYS292GLU
Human bek mRNA for fibroblast growth factor receptor-BEK	X52832	176943	TRP290ARG
Human bek mRNA for fibroblast growth factor receptor-BEK	X52832	176943	TRP290GLY
Human bek mRNA for fibroblast growth factor receptor-BEK	X52832	176943	VAL-VAL DEL
Human bek mRNA for fibroblast growth factor receptor-BEK	X52832	176943	SER351CYS
Human bek mRNA for fibroblast growth factor receptor-BEK	X52832	176943	SER252PHE
Human beta-LH gene (luteinizing hormone gene beta subunit)	X00264	152780	ILE15THR
Human beta-LH gene (luteinizing hormone	X00264	152780	TRP8ARG

SD-144141.1

gene beta subunit)	X00264	152780	GLN54ARG
Human beta-LH gene (lutinizizing hormone gene beta subunit)			
Human brain glycogen phosphorylase mRNA, complete cds	J03544	138550	none found
Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	1-BP INS, CODON 443
Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	1305G-C
Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	C1644i
Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	EX4-10DEL
Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	HindIII
Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	VAL458ALA
Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	R338L
Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	GLY340ARG

Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	ALA229THR
Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	THR332DEL
Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	ARG383HIS
Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	LYS438GLU
Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	GLY340SER
Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	ARG320LEU
Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	ARG311HIS
Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	ARG438HIS
Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	ARG320CYS
Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	ARG338TRP
Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	ALA312THR

SD-144141.1

for thyroid hormone receptor	X04707	190160	GLY327ARG
Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	GLY340VAL
Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	GLY342GLU
Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	MET437VAL
Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	PRO448THR
Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	PRO448HIS
Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	THR337ALA
Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	CYS434TER
Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	CYS446ARG
Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	LEU445HIS

SD-144141.1

receptor Human c-erb-A mRNA for thyroid hormone	X04707	190160	GLY340ASP
receptor Human c-erb-A mRNA for thyroid hormone	X04707	190160	GLN335HIS
receptor Human c-erb-A mRNA for thyroid hormone	X04707	190160	pro453ser
receptor Human c-erb-A mRNA for thyroid hormone	X04707	190160	R316H
receptor Human c-erb-A mRNA for thyroid hormone	X04707	190160	met313thre
receptor Human c-erb-A mRNA for thyroid hormone	X04707	190160	L346V
receptor Human c-erb-A mRNA for thyroid hormone	X04707	190160	MET310THR
receptor Human c-erb-A mRNA for thyroid hormone	X04707	190160	LEU325PHE
receptor Human c-erb-A mRNA for thyroid hormone	X04707	190160	ARG243GLN
receptor Human c-erb-A mRNA for thyroid hormone	X04707	190160	ARG243TRP

SD-144141.1

Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	ASP317HIS
Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	PHE454CYS
Human c-erb-A mRNA for thyroid hormone receptor	X04707	190160	ARG315HIS
Human c-erbA-1 mRNA for thyroid hormone receptor alpha	X55005	190120	LYS370ASN
Human c-erbA-1 mRNA for thyroid hormone receptor alpha	X55005	190120	SER377LEU
Human c-erbA-1 mRNA for thyroid hormone receptor alpha	X55005	190120	SER45ILE
Human cGMP- inhibited cAMP phosphodiesterase mRNA, complete cds	M91667	123805	none found
Human colipase mRNA, complete cds	J02883	120105	none found
Human collagen type XVIII alpha 1 (COL18A1) mRNA, partial cds	L22548	120328	none found
Human CYP11B2 gene for steroid 18- hydroxylase, complete	D13752	124080	-344C/T

Human CYP11B2 gene for steroid 18- hydroxylase, complete cds	D13752	124080	5-BP DEL	frameshift
Human CYP11B2 gene for steroid 18- hydroxylase, complete cds	D13752	124080	T4986C	
Human CYP11B2 gene for steroid 18- hydroxylase, complete cds	D13752	124080		GLU198ASP
Human CYP11B2 gene for steroid 18- hydroxylase, complete cds	D13752	124080		GLU255TER
Human CYP11B2 gene for steroid 18- hydroxylase, complete cds	D13752	124080		LYS173ARG
Human CYP11B2 gene for steroid 18- hydroxylase, complete cds	D13752	124080		THR185ILE
Human CYP11B2 gene for steroid 18- hydroxylase, complete cds	D13752	124080		LEU461PRO
Human CYP11B2 gene for steroid 18- hydroxylase, complete cds	D13752	124080		ARG181TRP

SD-144141.1

hydroxylase, complete cds				
Human CYP11B2 gene for steroid 18- hydroxylase, complete cds	D13752	124080		VAL386ALA
Human CYP11B2 gene for steroid 18- hydroxylase, complete cds	D13752	124080		T318M
Human cytochrome P450c21 mRNA, 3' end	M17252	201910	1761Tins	
Human cytochrome P450c21 mRNA, 3' end	M17252	201910	C-G intron 2	
Human cytochrome P450c21 mRNA, 3' end	M17252	201910	DEL	
Human cytochrome P450c21 mRNA, 3' end	M17252	201910	PvuII	
Human cytochrome P450c21 mRNA, 3' end	M17252	201910	TGC to AC	
Human cytochrome P450c21 mRNA, 3' end	M17252	201910	3-BP INS	LEU10INS
Human cytochrome P450c21 mRNA, 3' end	M17252	201910	656 A-->G	
Human cytochrome P450c21 mRNA, 3' end	M17252	201910	8-BP DEL	
Human cytochrome P450c21 mRNA, 3' end	M17252	201910	ClusterE6	
Human cytochrome P450c21 mRNA, 3' end	M17252	201910	F306+t	
Human cytochrome P450c21 mRNA, 3' end	M17252	201910	G-T exon 7	

SD-144141.1

P450c21 mRNA, 3' end	M17252	201910	GG dinucleotide to a C in exon 10	
Human cytochrome			HaeIII	
P450c21 mRNA, 3' end	M17252	201910	IVS2AS A/C-G, -13	
Human cytochrome			IVS7DS, G-C, +1	
P450c21 mRNA, 3' end	M17252	201910	NcoI	
Human cytochrome			Rsa I	
P450c21 mRNA, 3' end	M17252	201910	T-A exon 4	
Human cytochrome				ILE172ASN
P450c21 mRNA, 3' end	M17252	201910		VAL281LEU
Human cytochrome				PRO30LEU
P450c21 mRNA, 3' end	M17252	201910		SER268THR
Human cytochrome				GLY292SER
P450c21 mRNA, 3' end	M17252	201910		PRO453SER
Human cytochrome				TYR102ARG
P450c21 mRNA, 3' end	M17252	201910		ILE235ASN
Human cytochrome				

SD-144141.1

Human cytochrome P450c21 mRNA, 3' end	M17252	201910	VAL236GLU
Human cytochrome P450c21 mRNA, 3' end	M17252	201910	MET238LYS
Human cytochrome P450c21 mRNA, 3' end	M17252	201910	GLN318TER
Human cytochrome P450c21 mRNA, 3' end	M17252	201910	ARG339HIS
Human cytochrome P450c21 mRNA, 3' end	M17252	201910	TRP406TER
Human cytochrome P450c21 mRNA, 3' end	M17252	201910	GLU380ASP
Human cytochrome P450c21 mRNA, 3' end	M17252	201910	Q318X
Human cytochrome P450c21 mRNA, 3' end	M17252	201910	R356W
Human cytochrome P450c21 mRNA, 3' end	M17252	201910	I236N
Human cytochrome P450c21 mRNA, 3' end	M17252	201910	V237E
Human cytochrome P450c21 mRNA, 3' end	M17252	201910	M239K
Human cytochrome P450c21 mRNA, 3' end	M17252	201910	GLY524SER
Human cytochrome P450c21 mRNA, 3' end	M17252	201910	R356Q
Human cytochrome P450c21 mRNA, 3' end	M17252	201910	Y97X
Human cytochrome P450c21 mRNA, 3' end	M17252	201910	Arg357Trp
Human cytochrome P450c21 mRNA, 3' end	M17252	201910	D183E

SD-144141.1

P450c21 mRNA, 3' end	M17252	201910	W23X
Human cytochrome			
P450c21 mRNA, 3' end	U26644	600212	none found
Human fatty acid			
synthase (fas) mRNA,			
complete cds			
Human gene for	X52560	189965	none found
nuclear factor NF-IL6			
Human glucagon-like	U01157	138032	none found
peptide-1 receptor			
mRNA with CA			
dinucleotide repeat,			
complete cds			
Human heparin-	M32977	192240	none found
binding vascular			
endothelial growth			
factor (VEGF) mRNA,			
complete cds			
Human hepatic lipase	J03540	151670	SER267PHE
mRNA, complete cds			
Human hepatic lipase	J03540	151670	THR383MET
mRNA, complete cds			
Human hepatic nuclear	M57732	142410	A-C, -58
factor 1 (TCF1)			
mRNA, complete cds,			
clones HCL10,			
HCL12, HCL17, and			
HCL20			
Human hepatic nuclear	M57732	142410	1-BP DEL
factor 1 (TCF1)			frameshift
mRNA, complete cds,			

SD-144141.1

clones HCL10, HCL12, HCL17, and HCL20	M57732	142410	1-BP INS	frameshift
Human hepatic nuclear factor 1 (TCF1) mRNA, complete cds, clones HCL10, HCL12, HCL17, and HCL20	M57732	142410	RsaI promoter	
Human hepatic nuclear factor 1 (TCF1) mRNA, complete cds, clones HCL10, HCL12, HCL17, and HCL20	M57732	142410		PRO447LEU
Human hepatic nuclear factor 1 (TCF1) mRNA, complete cds, clones HCL10, HCL12, HCL17, and HCL20	M57732	142410		E619K
Human hepatic nuclear factor 1 (TCF1) mRNA, complete cds, clones HCL10, HCL12, HCL17, and HCL20	M57732	142410		R537T

SD-144141.1

HCL12, HCL17, and HCL20	M57732	142410	Ala/Val98
Human hepatic nuclear factor 1 (TCF1) mRNA, complete cds, clones HCL10, HCL12, HCL17, and HCL20			
Human hepatic nuclear factor 1 (TCF1) mRNA, complete cds, clones HCL10, HCL12, HCL17, and HCL20	M57732	142410	TYR122CYS
Human hepatic nuclear factor 1 (TCF1) mRNA, complete cds, clones HCL10, HCL12, HCL17, and HCL20	M57732	142410	THR620ILE
Human hepatic nuclear factor 1 (TCF1) mRNA, complete cds, clones HCL10, HCL12, HCL17, and HCL20	M57732	142410	Gly574Ser
Human hepatic nuclear factor 1 (TCF1) mRNA, complete cds, clones HCL10, HCL12, HCL17, and HCL20	M57732	142410	Cys241Gly

HCL20 Human hepatic nuclear factor 1 (TCF1) mRNA, complete cds, clones HCL10, HCL12, HCL17, and HCL20	M57732	142410	Glu48Lys
HCL20 Human hepatic nuclear factor 1 (TCF1) mRNA, complete cds, clones HCL10, HCL12, HCL17, and HCL20	M57732	142410	Pro291fsdelA
HCL20 Human hepatic nuclear factor 1 (TCF1) mRNA, complete cds, clones HCL10, HCL12, HCL17, and HCL20	M57732	142410	ARG272HIS
HCL20 Human hepatic nuclear factor 1 (TCF1) mRNA, complete cds, clones HCL10, HCL12, HCL17, and HCL20	M57732	142410	ARG583GLY
HCL20 Human hepatic nuclear factor 1 (TCF1) mRNA, complete cds, clones HCL10, HCL12, HCL17, and HCL20	M57732	142410	K205Q

Human hepatic nuclear factor 1 (TCF1) mRNA, complete cds, clones HCL10, HCL12, HCL17, and HCL20	M57732	142410	R131Q
Human hepatic nuclear factor 1 (TCF1) mRNA, complete cds, clones HCL10, HCL12, HCL17, and HCL20	M57732	142410	T392fsdelA
Human hepatic nuclear factor 1 (TCF1) mRNA, complete cds, clones HCL10, HCL12, HCL17, and HCL20	M57732	142410	L12H
Human hepatic nuclear factor 1 (TCF1) mRNA, complete cds, clones HCL10, HCL12, HCL17, and HCL20	M57732	142410	L584S585fsinsT C
Human hepatic nuclear factor 1 (TCF1) mRNA, complete cds, clones HCL10, HCL12, HCL17, and HCL20	M57732	142410	P379fsdelCT
Human hepatic nuclear factor 1 (TCF1) mRNA, complete cds, clones HCL10, HCL12, HCL17, and HCL20	M57732	142410	R263C

factor 1 (TCF1) mRNA, complete cds, clones HCL10, HCL12, HCL17, and HCL20	M57732	142410	G191D
Human hepatic nuclear factor 1 (TCF1) mRNA, complete cds, clones HCL10, HCL12, HCL17, and HCL20	M57732	142410	GLY319SER
Human hepatocyte nuclear factor-3 alpha (HNF-3 alpha) mRNA, complete cds	U39840	602294	none found
Human hormone- sensitive lipase testicular isoform mRNA, complete cds	U40002	151750	dinucleotide repeat
Human hormone- sensitive lipase testicular isoform mRNA, complete cds	U40002	151750	Arg309Cys
Human HXC-26 mRNA, complete cds	D83260	601125	none found

Human insulin promoter factor 1 (IPF1) mRNA, complete cds	U30329	600733	1-BP DEL	frameshift
Human insulin- degrading enzyme (IDE) mRNA, complete cds	M21188	146680	none found	
Human insulin- responsive glucose transporter (GLUT4) mRNA, complete cds	M20747	138190		VAL383ILE
Human liver glycogen phosphorylase type IV mRNA, 3' end	M36807	232700	IVS13DS, G-A, +1	
Human liver glycogen phosphorylase type IV mRNA, 3' end	M36807	232700	IVS14DS, G-A, +1	
Human liver glycogen phosphorylase type IV mRNA, 3' end	M36807	232700	IVS4AS, G-C, -1	
Human liver glycogen phosphorylase type IV mRNA, 3' end	M36807	232700		ASN338SER
Human liver glycogen phosphorylase type IV mRNA, 3' end	M36807	232700		ASN376LYS
Human liver glycogen phosphorylase type IV mRNA, 3' end	M36807	232700		VAL221ILE
Human long-chain	L09229	152425	A-->T	new initiation

SD-144141.1

acyl-coenzyme A synthetase (FACL1) mRNA, complete cds				codon +18 amino acids
Human luteinizing hormone- choriogonadotropin receptor mRNA, complete cds	M63108	152790	6-BP DEL, NT1822	
Human luteinizing hormone- choriogonadotropin receptor mRNA, complete cds	M63108	152790	LEU-GLN INS, CODON 19-20	
Human luteinizing hormone- choriogonadotropin receptor mRNA, complete cds	M63108	152790		SER616TYR
Human luteinizing hormone- choriogonadotropin receptor mRNA, complete cds	M63108	152790		ARG554TER
Human luteinizing hormone- choriogonadotropin receptor mRNA, complete cds	M63108	152790		ALA593PRO
Human luteinizing hormone- choriogonadotropin receptor mRNA, complete cds	M63108	152790		ASP578GLY

receptor mRNA, complete cds Human luteinizing hormone- choriogonadotropin receptor mRNA, complete cds	M63108	152790	ILE625LYS
Human luteinizing hormone- choriogonadotropin receptor mRNA, complete cds	M63108	152790	ILE542LEU
Human luteinizing hormone- choriogonadotropin receptor mRNA, complete cds	M63108	152790	ALA373VAL
Human luteinizing hormone- choriogonadotropin receptor mRNA, complete cds	M63108	152790	GLU354LYS
Human luteinizing hormone- choriogonadotropin receptor mRNA, complete cds	M63108	152790	ARG133CYS
Human luteinizing hormone- choriogonadotropin receptor mRNA, complete cds	M63108	152790	ASP578GLY

complete cds Human luteinizing hormone- choriogonadotropin receptor mRNA, complete cds	M63108	152790	ALA572VAL
Human luteinizing hormone- choriogonadotropin receptor mRNA, complete cds	M63108	152790	THR577ILE
Human luteinizing hormone- choriogonadotropin receptor mRNA, complete cds	M63108	152790	ASP582GLY
Human luteinizing hormone- choriogonadotropin receptor mRNA, complete cds	M63108	152790	MET575ILE
Human luteinizing hormone- choriogonadotropin receptor mRNA, complete cds	M63108	152790	MET398THR
Human luteinizing hormone- choriogonadotropin receptor mRNA, complete cds	M63108	152790	CYSS45TER

Human metalloendopeptidase homolog (PEX) mRNA, partial cds	U60475	307800	2-BP DEL	frameshift
Human metalloendopeptidase homolog (PEX) mRNA, partial cds	U60475	307800	A-G, NT-429	
Human metalloendopeptidase homolog (PEX) mRNA, partial cds	U60475	307800	IVS1AS, G-A, -1	
Human metalloendopeptidase homolog (PEX) mRNA, partial cds	U60475	307800	IVS1AS, G-C, -1	
Human metalloendopeptidase homolog (PEX) mRNA, partial cds	U60475	307800		LEU555PRO
Human metalloendopeptidase homolog (PEX) mRNA, partial cds	U60475	307800		CYS82TYR
Human metalloendopeptidase homolog (PEX) mRNA, partial cds	U60475	307800		LEU274TER
Human metalloendopeptidase homolog (PEX)	U60475	307800		MET250ILE

mRNA, partial cds Human metalloendopeptidase homolog (PEX)	U60475	307800		PHE249SER
mRNA, partial cds Human molecular marker (EPC-1) gene, complete cds	M90439	172860	G to A 5	
Human molecular marker (EPC-1) gene, complete cds	M90439	172860		Met72Thr
Human molecular marker (EPC-1) gene, complete cds	M90439	172860		Thr130Thr
Human molecular marker (EPC-1) gene, complete cds	M90439	172860		Tyr321Tyr
Human mRNA for alpha-tocopherol transfer protein, complete cds	D49488	600415	1-BP DEL 744	
Human mRNA for alpha-tocopherol transfer protein, complete cds	D49488	600415	1-BP DEL, 485T	frameshift
Human mRNA for alpha-tocopherol transfer protein, complete cds	D49488	600415	2-BP INS, 513TT	
Human mRNA for alpha-tocopherol transfer protein, complete cds	D49488	600415	552G-A	

SD-144141.1

transfer protein, complete cds	D49488	600415	HIS101GLN
Human mRNA for alpha-tocopherol transfer protein, complete cds	D49488	600415	ARG192HIS
Human mRNA for alpha-tocopherol transfer protein, complete cds	D49488	600415	ARG134TER
Human mRNA for carboxypeptidase E (EC 3.4.17.10)	X51405	114855	none found
Human mRNA for cytochrome P-450 (11 Beta)	X55764	202010	2-BP INS, CODON 394 frameshift
Human mRNA for cytochrome P-450 (11 Beta)	X55764	202010	28bp deletion
Human mRNA for cytochrome P-450 (11 Beta)	X55764	202010	5 bp duplication
Human mRNA for cytochrome P-450 (11 Beta)	X55764	202010	CHIMERA
Human mRNA for cytochrome P-450 (11 Beta)	X55764	202010	MspI

SD-144141.1

Beta) Human mRNA for cytochrome P-450 (11	X55764	202010	PvuII	
Beta) Human mRNA for cytochrome P-450 (11	X55764	202010		ARG448HIS
Beta) Human mRNA for cytochrome P-450 (11	X55764	202010		TRP116TER
Beta) Human mRNA for cytochrome P-450 (11	X55764	202010		N133H
Beta) Human mRNA for cytochrome P-450 (11	X55764	202010		P42S
Beta) Human mRNA for cytochrome P-450 (11	X55764	202010		Y423X
Beta) Human mRNA for cytochrome P-450 (11	X55764	202010		arg384gly
Beta) Human mRNA for cytochrome P-450 (11	X55764	202010		ARG374GLN
Beta) Human mRNA for cytochrome P-450 (11	X55764	202010		THR318MET
Beta) Human mRNA for cytochrome P-450 (11	X55764	202010		C494F

SD-144141.1

Human mRNA for cytochrome P-450 (11 Beta)	X55764	202010		G267D
Human mRNA for cytochrome P-450 (11 Beta)	X55764	202010		G267R
Human mRNA for cytochrome P-450 (11 Beta)	X55764	202010		Q356X
Human mRNA for cytochrome P-450 (11 Beta)	X55764	202010		R427H
Human mRNA for glioblastoma-derived T-cell suppressor factor G-TsF (transforming growth factor-beta2, TGF-beta2)	Y00083	190220	none found	
Human mRNA for plasminogen	X05199	173350	IVS17, 1-BP DEL, G, +1 TaqI	
Human mRNA for plasminogen	X05199	173350		GLU460TER
Human mRNA for plasminogen	X05199	173350		ALA600THR
Human mRNA for plasminogen	X05199	173350		ARG216HIS
Human mRNA for plasminogen	X05199	173350		GLY732ARG
Human mRNA for plasminogen	X05199	173350		LYS19GLU

SD-144141.1

Human plasminogen mRNA	X05199	173350	LYS212DEL
Human plasminogen mRNA	X05199	173350	SER572PRO
Human plasminogen mRNA	X05199	173350	TRP597TER
Human plasminogen mRNA	X05199	173350	VAL355PHE
Human plasminogen mRNA	X05199	173350	D676N
Human plasminogen mRNA	X05199	173350	Ala675Thr
Human transforming growth factor-beta (TGF-beta) mRNA	X02812	190180	713-8delC
Human transforming growth factor-beta (TGF-beta) mRNA	X02812	190180	Leu10-->Pro
Human transforming growth factor-beta (TGF-beta) mRNA	X02812	190180	Arg25-->Pro
Human transforming growth factor-beta 3 (TGF-beta 3) mRNA	X14149	190230	none found
Human variant hepatic nuclear factor 1 (vHNF1) mRNA	X58840	189907	75-BP DEL, NT409
Human variant hepatic nuclear factor 1 (vHNF1) mRNA	X58840	189907	ARG177TER

factor 1 (vHNF1)				
Human mRNA fragment for second calcitonin gene related peptide (CGRP) from medullary thyroid carcinoma (MTC)	X02404	114160	none found	
Human mRNA for pro-cathepsin L (major excreted protein MEP)	X12451	116880	none found	
Human muscle glycogen synthase mRNA, complete cds	J04501	138570	TTC342TTT	
Human muscle glycogen synthase mRNA, complete cds	J04501	138570		Gln71His
Human muscle glycogen synthase mRNA, complete cds	J04501	138570		Gly464Ser
Human muscle glycogen synthase mRNA, complete cds	J04501	138570		Met416Val
Human myeloid- specific C/EBP-epsilon transcription factor (CEBPE) gene, complete cds	U80982	600749	none found	
Human neurokinin A receptor (NK-2R) mRNA, complete cds	M57414	162321	none found	
Human NF-IL6-beta	M83667	116898	none found	

SD-144141.1

protein mRNA, complete cds				
Human obese (ob) mRNA, complete cds	U18915	164160	-1387 G/A	
Human obese (ob) mRNA, complete cds	U18915	164160	1-BP DEL	frameshift
Human obese (ob) mRNA, complete cds	U18915	164160	A --> G + 19 exon1	
Human obese (ob) mRNA, complete cds	U18915	164160	C(-188)A	
Human obese (ob) mRNA, complete cds	U18915	164160		ARG105TRP
Human obese (ob) mRNA, complete cds	U18915	164160		Glu-126-Gln
Human obese (ob) mRNA, complete cds	U18915	164160		Ser-91-Ser
Human pancreatic beta-cell glucokinase mRNA, complete cds	M88011	138079	CCC[Pro]-- >CCG[Pro] at codon 145	
Human pancreatic beta-cell glucokinase mRNA, complete cds	M88011	138079	intron 1 a variant (C-->T)	
Human pancreatic beta-cell glucokinase mRNA, complete cds	M88011	138079	(-258) G-to-A	
Human pancreatic beta-cell glucokinase mRNA, complete cds	M88011	138079	(TAC-->TAT) in codon 215	
Human pancreatic beta-cell glucokinase mRNA, complete cds	M88011	138079	-120 (G-->T)	

SD-144141.1

Human pancreatic beta-cell glucokinase mRNA, complete cds	M88011	138079	-194 (A-->G)
Human pancreatic beta-cell glucokinase mRNA, complete cds	M88011	138079	-282 (C-->T)
Human pancreatic beta-cell glucokinase mRNA, complete cds	M88011	138079	-30 G/A
Human pancreatic beta-cell glucokinase mRNA, complete cds	M88011	138079	10-bp (base pair) deletion in exon 3;
Human pancreatic beta-cell glucokinase mRNA, complete cds	M88011	138079	33-bp deletion at the exon 5/intron 5 junction 403 (C-->G)
Human pancreatic beta-cell glucokinase mRNA, complete cds	M88011	138079	603 (G-->T)
Human pancreatic beta-cell glucokinase mRNA, complete cds	M88011	138079	A--> G 244
Human pancreatic beta-cell glucokinase mRNA, complete cds	M88011	138079	C--> T 8 bp 3' to the exon 9
Human pancreatic beta-cell glucokinase mRNA, complete cds	M88011	138079	compound imperfect dinucleotide repeat
Human pancreatic beta-cell glucokinase mRNA, complete cds	M88011	138079	G--> A 13

SD-144141.1

beta-cell glucokinase mRNA, complete cds	M88011	138079	IVS4DS, 15-BP DEL	
Human pancreatic beta-cell glucokinase mRNA, complete cds	M88011	138079	TGG257-->CGG257	
Human pancreatic beta-cell glucokinase mRNA, complete cds	M88011	138079		ARG186TER
Human pancreatic beta-cell glucokinase mRNA, complete cds	M88011	138079		GLU265TER
Human pancreatic beta-cell glucokinase mRNA, complete cds	M88011	138079		GLU279TER
Human pancreatic beta-cell glucokinase mRNA, complete cds	M88011	138079		GLY261ARG
Human pancreatic beta-cell glucokinase mRNA, complete cds	M88011	138079		GLY299ARG
Human pancreatic beta-cell glucokinase mRNA, complete cds	M88011	138079		SER131PRO
Human pancreatic beta-cell glucokinase mRNA, complete cds	M88011	138079		THR228MET
Human pancreatic beta-cell glucokinase mRNA, complete cds	M88011	138079		VAL455MET

SD-144141.1

mRNA, complete cds				
Human pancreatic	M88011	138079		Val62Ala
beta-cell glucokinase				
mRNA, complete cds				
Human pancreatic	M88011	138079		Thr209--
beta-cell glucokinase				>Met209
mRNA, complete cds				
Human pancreatic	M88011	138079		Gly261--
beta-cell glucokinase				>Glu261
mRNA, complete cds				
Human pancreatic	M88011	138079		Arg36-->Trp36
beta-cell glucokinase				
mRNA, complete cds				
Human pancreatic	M88011	138079		Glu70-->Lys
beta-cell glucokinase				
mRNA, complete cds				
Human pancreatic	M88011	138079		Ser131-->Pro
beta-cell glucokinase				
mRNA, complete cds				
Human pancreatic	M88011	138079		Ala188-->Thr
beta-cell glucokinase				
mRNA, complete cds				
Human pancreatic	M88011	138079		Trp257-->Arg
beta-cell glucokinase				
mRNA, complete cds				
Human pancreatic	M88011	138079		Lys414-->Glu
beta-cell glucokinase				
mRNA, complete cds				
Human pancreatic	M88011	138079		Asp4-->Asn
beta-cell glucokinase				
mRNA, complete cds				

SD-144141.1

Human pancreatic beta-cell glucokinase mRNA, complete cds	M88011	138079	Ala11Thr
Human parathyroid cell calcium-sensing receptor mRNA, complete cds	U20759	601199	(CA)n
Human parathyroid cell calcium-sensing receptor mRNA, complete cds	U20759	601199	2-BP DEL/1-BP INS
Human parathyroid cell calcium-sensing receptor mRNA, complete cds	U20759	601199	ALU INS, CODON 877
Human parathyroid cell calcium-sensing receptor mRNA, complete cds	U20759	601199	T/C fifth intron
Human parathyroid cell calcium-sensing receptor mRNA, complete cds	U20759	601199	ARG796TRP
Human parathyroid cell calcium-sensing receptor mRNA, complete cds	U20759	601199	GLU298LYS
Human parathyroid cell calcium-sensing receptor mRNA, complete cds	U20759	601199	ARG185GLN

Human parathyroid cell calcium-sensing receptor mRNA, complete cds	U20759	601199	GLU128ALA
Human parathyroid cell calcium-sensing receptor mRNA, complete cds	U20759	601199	ARG227LEU
Human parathyroid cell calcium-sensing receptor mRNA, complete cds	U20759	601199	CYS582TYR
Human parathyroid cell calcium-sensing receptor mRNA, complete cds	U20759	601199	GLU681HIS
Human parathyroid cell calcium-sensing receptor mRNA, complete cds	U20759	601199	ALA116THR
Human parathyroid cell calcium-sensing receptor mRNA, complete cds	U20759	601199	PHE806SER
Human parathyroid cell calcium-sensing receptor mRNA, complete cds	U20759	601199	THR151MET
Human parathyroid cell calcium-sensing receptor mRNA,	U20759	601199	ASN118LYS

SD-144141.1

complete cds Human parathyroid cell calcium-sensing receptor mRNA, complete cds	U20759	601199	PHE128LEU
Human parathyroid cell calcium-sensing receptor mRNA, complete cds	U20759	601199	THR151MET
Human parathyroid cell calcium-sensing receptor mRNA, complete cds	U20759	601199	GLU191LYS
Human parathyroid cell calcium-sensing receptor mRNA, complete cds	U20759	601199	PHE612SER
Human parathyroid cell calcium-sensing receptor mRNA, complete cds	U20759	601199	LEU773ARG
Human parathyroid cell calcium-sensing receptor mRNA, complete cds	U20759	601199	ARG185TER
Human parathyroid cell calcium-sensing receptor mRNA, complete cds	U20759	601199	GLY670GLU
Human parathyroid cell calcium-sensing receptor mRNA, complete cds	U20759	601199	PRO40ALA

SD-144141.1

receptor mRNA, complete cds	U20759	601199	ARG228GLN
Human parathyroid cell calcium-sensing receptor mRNA, complete cds	U20759	601199	THR139MET
Human parathyroid cell calcium-sensing receptor mRNA, complete cds	U20759	601199	GLY144GLU
Human parathyroid cell calcium-sensing receptor mRNA, complete cds	U20759	601199	ARG63MET
Human parathyroid cell calcium-sensing receptor mRNA, complete cds	U20759	601199	ARG67CYS
Human parathyroid cell calcium-sensing receptor mRNA, complete cds	U20759	601199	PHE788CYS
Human parathyroid cell calcium-sensing receptor mRNA, complete cds	U20759	601199	LYS47ASN
Human parathyroid cell calcium-sensing receptor mRNA, complete cds	U20759	601199	A986S

SD-144141.1

calcium-sensing receptor mRNA, complete cds	U43148	601309	1148G-A	
Human patched homolog (PTC) mRNA, complete cds	U43148	601309	1-BP DEL	
Human patched homolog (PTC) mRNA, complete cds	U43148	601309	1-BP INS	
Human patched homolog (PTC) mRNA, complete cds	U43148	601309	11-BP DEL	frameshift
Human patched homolog (PTC) mRNA, complete cds	U43148	601309	2-BP INS	
Human patched homolog (PTC) mRNA, complete cds	U43148	601309	3340A-T	
Human patched homolog (PTC) mRNA, complete cds	U43148	601309	37-BP DEL	
Human patched homolog (PTC) mRNA, complete cds	U43148	601309	451C-T	Pro-Ser
Human patched homolog (PTC) mRNA, complete cds	U43148	601309	9-BP INS	CODON 815, PRO-ASN-ILE INS nonsense
Human patched homolog (PTC) mRNA, complete cds	U43148	601309	CAG to TAG at	

SD-144141.1

homolog (PTC) mRNA, complete cds	U43148	601309	codon 361	GLN210TER
Human patched homolog (PTC) mRNA, complete cds	U43148	601309		Gln816Leu
Human patched homolog (PTC) mRNA, complete cds	U25128	601469	none found	
Human PTH2 parathyroid hormone receptor mRNA, complete cds	U47050	602345	none found	
Human putative calcium influx channel (htrp3) mRNA, complete cds	M91211	600214	none found	
Human receptor for advanced glycosylation end products (RAGE) mRNA, partial cds	M12654	139200	HaeIII	
Human serum vitamin D-binding protein (hDBP) mRNA, complete cds	M12654	139200	(TAAA)n	
Human serum vitamin D-binding protein (hDBP) mRNA, complete cds	M12654	139200	MspI	
Human serum vitamin D-binding protein (hDBP) mRNA,				

SD-144141.1

complete cds				
Human serum vitamin D-binding protein (hDBP) mRNA, complete cds	M12654	139200	Styl	
Human serum vitamin D-binding protein (hDBP) mRNA, complete cds	M12654	139200	T to C at Cys283	
Human serum vitamin D-binding protein (hDBP) mRNA, complete cds	M12654	139200		THR420LYS
Human somatostatin I gene and flanks	J00306	182450	BamHI intron	
Human somatostatin I gene and flanks	J00306	182450	EcoRI 3'	
Human SREBP-1 mRNA, complete cds	U00968	184756	none found	
Human stanniocalcin mRNA, complete cds	U46768	601185	none found	
Human steroid 5-alpha-reductase 2 (SRD5A2) mRNA, complete cds	M74047	264600	1-BP DEL	PRO251DEL
Human steroid 5-alpha-reductase 2 (SRD5A2) mRNA, complete cds	M74047	264600	null allele	
Human steroid 5-alpha-reductase 2 (SRD5A2) mRNA, complete cds	M74047	264600		ARG246TRP
Human steroid 5-alpha-reductase 2 (SRD5A2) mRNA, complete cds	M74047	264600		GLY115ASP

reductase 2 (SRD5A2) mRNA, complete cds	M74047	264600	GLY183SER
Human steroid 5-alpha- reductase 2 (SRD5A2) mRNA, complete cds	M74047	264600	GLY196SER
Human steroid 5-alpha- reductase 2 (SRD5A2) mRNA, complete cds	M74047	264600	HIS231ARG
Human steroid 5-alpha- reductase 2 (SRD5A2) mRNA, complete cds	M74047	264600	LEU55GLN
Human steroid 5-alpha- reductase 2 (SRD5A2) mRNA, complete cds	M74047	264600	MET157DEL
Human steroid 5-alpha- reductase 2 (SRD5A2) mRNA, complete cds	M74047	264600	THR228ALA
Human steroid 5-alpha- reductase 2 (SRD5A2) mRNA, complete cds	M74047	264600	ARG227TER
Human steroidogenic acute regulatory protein (StAR) mRNA, complete cds	U17280	600617	840delA
Human steroidogenic acute regulatory protein (StAR) mRNA, complete cds	U17280	600617	IVS4AS, T-A, -11

SD-144141.1

Human steroidogenic acute regulatory protein (StAR) mRNA, complete cds	U17280	600617	GLN258TER
Human steroidogenic acute regulatory protein (StAR) mRNA, complete cds	U17280	600617	ARG182LEU
Human steroidogenic acute regulatory protein (StAR) mRNA, complete cds	U17280	600617	1-BP DEL, 261T
Human steroidogenic acute regulatory protein (StAR) mRNA, complete cds	U17280	600617	IVS2, 1-BP INS, T, +3
Human steroidogenic acute regulatory protein (StAR) mRNA, complete cds	U17280	600617	D203A
Human sterol regulatory element binding protein-2 mRNA, complete cds	U02031	600481	none found
Human transforming growth factor-beta type III receptor (TGF-beta) mRNA, complete cds	L07594	600742	none found
Human type II iodothyronine deiodinase mRNA,	U53506	601413	none found

complete cds	U20165	600799	none found	
Human type II serine/threonine kinase receptor mRNA, complete cds	U43142	601528	none found	
Human vascular endothelial growth factor related protein VRP mRNA, complete cds	U43368	601398	none found	
Human VEGF related factor isoform VRF186 precursor (VRF)	M67466	201810	1-BP INS	
mRNA, complete cds				
Hydroxy-delta-5- steroid dehydrogenase, 3 beta- and steroid delta-isomerase 2	M67466	201810	Dinucleotide repeat	
Hydroxy-delta-5- steroid dehydrogenase, 3 beta- and steroid delta-isomerase 2	M67466	201810		ARG249TER
Hydroxy-delta-5- steroid dehydrogenase, 3 beta- and steroid delta-isomerase 2	M67466	201810		VAL248ASN
Hydroxy-delta-5- steroid dehydrogenase, 3 beta- and steroid delta-isomerase 2	M67466	201810		TRP171TER

[illegible]

Insulin receptor	M10051	147670	Gln276 (CAA-->CAG)	silent
Insulin receptor	M10051	147670	Gly8 (GGA-->GGG)	silent
Insulin receptor	M10051	147670	His1068 (CAC-->CAT)	silent
Insulin receptor	M10051	147670	Insertion intron 9,	
Insulin receptor	M10051	147670	Nsil	
Insulin receptor	M10051	147670	Nsil	
Insulin receptor	M10051	147670	Short repeats in intron 2	
Insulin receptor	M10051	147670	Thr789 (ACG-->ACA)	silent
Insulin receptor	M10051	147670		GLY996VAL
Insulin receptor	M10051	147670		GLU672TER
Insulin receptor	M10051	147670		LYS460GLU
Insulin receptor	M10051	147670		Asn461Thr
Insulin receptor	M10051	147670		MET1153ILE
Insulin receptor	M10051	147670		ARG86PRO
Insulin receptor	M10051	147670		TRP1200SER
Insulin receptor	M10051	147670		TRP?SER
Insulin receptor	M10051	147670		ALA1134THR
Insulin receptor	M10051	147670		LYS121TER
Insulin receptor	M10051	147670		ILE119MET
Insulin receptor	M10051	147670		ARG735SER
Insulin receptor	M10051	147670		ARG981GLN
Insulin receptor	M10051	147670		ARG988TER
Insulin receptor	M10051	147670		TRP412SER
Insulin receptor	M10051	147670		ALA1135GLU
Insulin receptor	M10051	147670		ARG1000TER
Insulin receptor	M10051	147670		ASN462SER
Insulin receptor	M10051	147670		CODON 897

Insulin receptor	M10051	147670	nonsense
Insulin receptor	M10051	147670	HIS209ARG
Insulin receptor	M10051	147670	TRP133TER
Insulin receptor	M10051	147670	Asn281del
Insulin receptor	M10051	147670	his252arg
Insulin receptor	M10051	147670	Leu999del
Insulin receptor	M10051	147670	glyc1008val
Insulin receptor	M10051	147670	glu1131arg
Insulin receptor	M10051	147670	Leu193Pro
Insulin receptor	M10051	147670	ser462asp
Insulin receptor	M10051	147670	GLY31ARG
Insulin receptor	M10051	147670	PHE382VAL
Insulin receptor	M10051	147670	LEU233PRO
Insulin receptor	M10051	147670	Arg86ter
Insulin receptor	M10051	147670	Trp1193Leu
Insulin receptor	M10051	147670	Leu1178Pro
Insulin receptor	M10051	147670	ARG1174GLN
Insulin receptor	M10051	147670	VAL985MET
Insulin receptor	M10051	147670	GLY366ARG
Insulin receptor	M10051	147670	VAL28ALA
Insulin receptor	M10051	147670	Asp59Gly
Insulin receptor	M10051	147670	Leu62Pro
Insulin receptor	M10051	147670	ARG372TER
Insulin receptor	M10051	147670	ASN15LYS
Insulin receptor	M10051	147670	ARG1152GLN
Insulin-like growth factor 1 receptor	X04434	147370	none found
Insulin-like growth factor 2	J03242	147470	(CA)n
Insulin-like growth factor 2	J03242	147470	Apal 3'UTR

Insulin-like growth factor 2	J03242	147470	Avall
Insulin-like growth factor 2	J03242	147470	BamHI
Insulin-like growth factor 2	J03242	147470	Eco RI
Insulin-like growth factor 2	J03242	147470	Sst I
Insulin-like growth factor 2	J03242	147470	VNTR upstream
insulin-like growth factor binding protein 1	NM_000596	146730	none found
Insulin-like growth factor1	M29644	147440	(CA) _n
Insulin-like growth factor1	M29644	147440	EcoRV
Insulin-like growth factor1	M29644	147440	EX4,5 DEL
Insulin-like growth factor1	M29644	147440	HindIII
Insulin-like growth factor1	M29644	147440	PvuII
interleukin 1 receptor (IL-1R)	M27492	147810	PstI
interleukin 6 receptor (IL-6R) (20)	M20566	147880	dinucleotide (CA)
inward rectifier K channel	D50582		none found
leptin receptor/LEPR	NM_002303	601007	(CTTTA) _n
leptin receptor/LEPR	NM_0023	601007	3'-UTR

SD-144141.1